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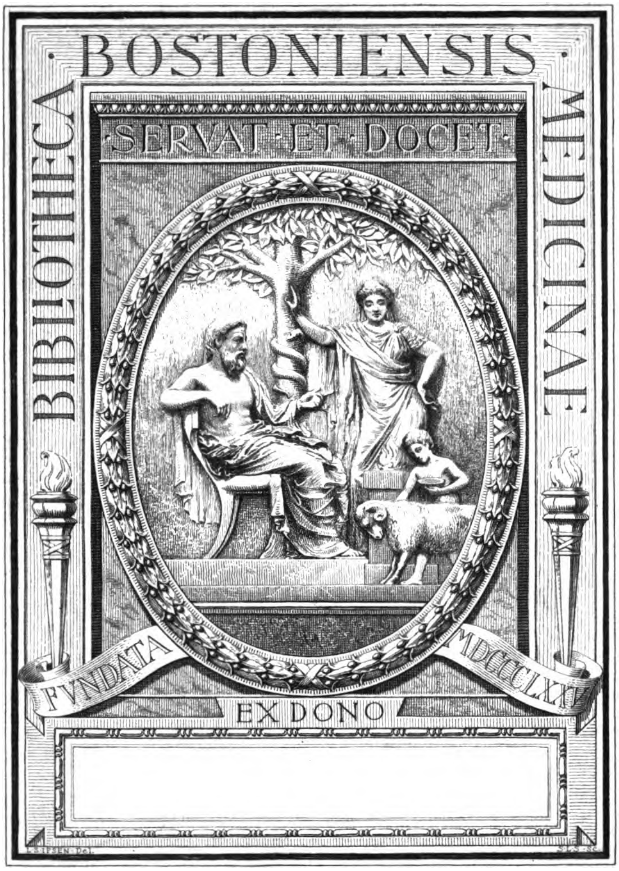

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Dr. James Ewing, *President.*

THE SIGNIFICANCE OF INTRAMEDULLARY DEGENERATIONS.

M. G. SCHLAPP, M.D.

At a recent meeting of this Society, I presented sections through the spinal cord, medulla, pons, and through the region of the neucleus of the third nerve, in a case of tumor of the right hemisphere of the cerebellum. These sections were presented in order to show degenerations in the posterior columns (which have been described by other writers), and similar degenerations in the intramedullary fibres of the sensory cranial nerves which, to my knowledge, have not been described before.

The specimens which I am showing you to-night are in addition to the aforesaid sections of the cerebellar case, transverse sections of the spinal cord of 1st.—A case of crushed cord. In this case the spinal cord was crushed in the region between the 6th and 7th dorsal vertebræ, absolutely destroying the cord in this region. If you will examine the sections of this case, which were taken from the lumbar and sacral regions, you will see that the posterior root-zone of Flechsig shows a marked degeneration. This degeneration can be followed to a point where the posterior root leaves the spinal cord, sometimes a little beyond; and if you will look closely you will see that this degeneration always stops, with the exception of a very few fibres, where the sheath of Schwann begins. These degenerated fibres are all ascending fibres and short ones, because they enter the gray matter where they seem to end.

2nd.—A case of transverse myelitis in the cervical region. In this case as in the crushed cord case, the posterior root-zone was markedly degenerated in the dorsal, lumbar and sacral regions.

3rd.—A case of alcoholic polyneuritis in combination with mental disturbances (described by Korsakow). In this case the degeneration was also well-marked in the posterior root-zone. The degeneration, however, was also found in other parts of the spinal cord, which I shall report later.

In all these four cases:

Cerebellar tumor case;
Crushed cord case. Lesion in the middle dorsal region;
Transverse myelitis case. Lesion in cervical region;
Alcoholic polyneuritis;

a marked lesion was found in the posterior root-zone. In the alcoholic case the nerves were involved; in the cases of transverse lesions of the cord, the descending tracts were all involved below the lesion; in the brain tumor case, the degeneration was almost entirely confined to the columns of Burdach, and especially in the posterior root-zone, a few degenerated fibres in the columns of Goll. The tendon and skin reflexes were missing below the lesion in the cases of transverse lesion of the cord. In the alcoholic case they were missing in the legs and lower part of the body, in the arms they were very much diminished, sometimes not obtainable, shortly before death missing. In the brain tumor case, they were entirely missing a few weeks before death.

Much has been written about the condition of the reflexes in cases of transverse lesion of the spinal cord. Bastian was the first, I think, to call attention to the absolute loss of the tendon reflexes of the legs in cases of transverse lesion of the cord in the cervical or upper dorsal regions. His explanation of the loss of the reflexes in the above conditions is that in a complete lesion of the cord the fibres which are constantly transmitting a stimulus from the cerebellum to the motor cells in the anterior horns of the spinal cord, whereby the muscles are kept in a normal tonic condition, are cut and this constant stimulus cannot reach the motor cells lying below the lesion, hence the muscles connected with these cells are not in a normal tonic state. Therefore, the reflexes which depend upon this tonic state are lost in the muscles involved. Recently cases have been described in which there were absolute transverse lesions of the cord in the cervical and dorsal regions with reflexes present or exaggerated below the lesion. The case of Kausch is especially important in demonstrating this fact. So the hypothesis of

Bastian cannot be accepted. The degeneration of the nerve fibres in the posterior root-zone of Flechsig no doubt explains the absence of the reflexes in these cases. In the alcoholic polyneuritis, the changes in the nerves could in themselves be sufficient to cause the loss of the reflexes, but the degenerations in the nerves are not so marked as the degenerations in the posterior root-zone of Flechsig.

It seems that the short fibres entering the cord through the posterior roots, or reflex fibres, are the ones in which the degeneration first takes place. Or in other words, they cannot withstand the effects of toxic substances or imperfect circulation as well as the fibres that carry the sensory impressions to the higher centres. This is also supported by clinical observations; that is, the absence of the reflexes is usually the first symptom of a disease in which the posterior columns are affected:—Tabes Dorsalis, ergot poisoning, brain tumor, etc. If the cause producing these degenerations continues long enough then of course the fibres transmitting the sensory impressions to higher centers will also degenerate, and we will then have a disturbance of sensation.

These cases will be published in full very soon.

A LYMPHOCYTOZOON OF THE GUINEA-PIG.

L. B. GOLDHORN, M.D.

While examining the blood of a certain guinea-pig, I found in the cytoplasm of a large number of lymphocytes highly refractive, round or elipsoid, non-motile bodies which when stained with ordinary methylene blue looked like vacuoles. As the nucleus of these cells was considerably displaced and undergoing karyorrhexis according to the size of the vacuoles, it was suspected that a parasite was present. Upon staining smears with polychrome methylene blue a brilliantly stained body was seen, varying in size from a barely visible dot to more than the size of the nucleus of the lymphocyte. While it frequently filled the space in the lymphocyte completely, it would as frequently appear surrounded by a sharply defined achromatic zone. This latter appearance was rather constant with the small forms.

It was assumed that if this body were a parasite it might be transmitted by inoculation. Intravenous injection was made into one young guinea-pig, while a second one received an equal amount of blood intraperitoneally; and into a third one a subcutaneous injection was made. One control pig was kept with these young ones, and all were isolated from the old infected pig. The transfused blood was suspended in physiological salt solution. All the animals were first carefully examined for abnormalities in the lymphocytes with negative results. It was thought best to take young animals since old animals appeared to show the bodies above described in nearly half the number examined.

At first, blood examinations of the inoculated pigs were made daily with entirely negative results; at the expiration of three weeks very diminutive bodies surrounded by a clear space were seen in the cytoplasm of the lymphocytes of the pig in which the injection had been made intravenously. The nucleus of such lymphocytes did not show any degenerative change. Three weeks later the the parasites had increased to twice their first size, but numerically they were not increased. At the very best few could be found.

The animal on which these observations were made showed as many infected lymphocytes as normal ones.

It was a pregnant female. The two young ones did not show at birth (nor do they show to this day) lymphocytes containing parasitic bodies.

Lymphocytes frequently showed more than one parasite. The only way of telling the small forms from the metachromatically staining bodies so frequently seen in the cytoplasm of lymphocytes was by observing the clear space surrounding the parasitic bodies. In multiple infection of one cell one parasite was not infrequeutly observed to be larger than others in the same cell. Two parasites maturing side by side were seen from time to time. I did not succeed in demonstrating anything in the clear space surrounding the very small forms; but this was very different with the large ones. In the first place it was noticed that the latter frequently have a more compact central body. The largest forms consisted of a loosened chromatin body surrounded by a meshwork which occupied frequently the entire achromatic zone mentioned. I have come to the conclusion that this clear zone is at all times made up of a substance the nature of which is still undetermined. I succeeded in finding a couple of extra cellular bodies surrounded by a sharply defined envelop corresponding in width to the achromatic area of half grown intra-cellular forms. In other instances lymphocytes injured in spreading the blood were found to have discharged their parasite which was found lying free in plasma, surrounded by a meshwork.

It is probable that Kurloff's cells with vacuoles are those described in this paper, and therefore I give in full the quotation by Ehrlich, since the original by Kurloff is in Russian. He says:

"This is a quite peculiar group, characteristic for the blood of the guinea-pig. It shows transitions in the blood from large mononuclear to transitional and polynuclear forms, but is marked by the lack of any kind of granulation. Instead of the latter we find in these cells a roundish, nucleus-like form in the protoplasm, which also takes the nuclear stains, and possibly is to be considered an accessory nucleus. We have received the impression that we have here to deal with a vacuole filled with substance secreted by the cell. In a large series of preparations, it is possible to obtain some elucidation of the development and fate of these appearances. They first appear in point-like granules in the protoplasm, bearing no relation to the cell-nucleus; they gradually increase and acquire a considerable circumference. When they have attained about the size of the cell-nucleus, they, or rather their contents, appear to break through the protoplasmic membrane and to leave the cell. The number of the vacuoles containing cells is 15 to 20% of the colorless blood corpuscles."

Cells with wide meshes in their cytoplasm simulating vacuoles are not infrequently seen in smears, but they are altogether unlike the bodies in question. To regard this body as an accessory nucleus is out of the question. It is seen at times outside of the cell as already stated, and is then frequently sharply outlined by a more or less achromatic zone. Moreover, its affinity for stains is altogether unlike that of the nucleus of the lymphocytes, and it stains best metachromatically.

The statement that vacuoles containing cells of the normal guinea-pig number 15 to 20% of the colorless corpuscles is an error if Kurloff's vacuoles are identical with the bodies described because there are many guinea pigs, if not the majority of them, that are free from such bodies.

If they are really parasites it may be desirable to examine the blood of guinea-pigs which are to be used for serum reactions to determine if they are heavily infected, as they then might occasionally alter such reactions.

I shall be thankful for suggestions as to the nature of these bodies. A microscopic examination of the tissues from guinea-pigs whose lymphocytes contained these bodies showed that there were in the alveoli of the thyroid gland what appeared to be foreign bodies, sometimes closely resembling encysted parasites; between the epithelial cells lining the alveoli, smaller foreign bodies were also seen. Future investigation will show how constant these changes are. The bone marrow was seen to contain the bodies in lymphocytes in large numbers. The technique was as follows:

Smear were fixed in wood alcohol for 15 to 30 seconds, and then washed in water until the water adheres to the smears. The preparations were stained in polychrome methylene blue (Goldhorn) for a few seconds, long enough to have the smears look grayish or bluish, and they were then washed thoroughly in clean water. Finally they were stained in .1% eosin for from 15 to 30 seconds, and washed again. Short eosin staining will leave the red corpuscles greenish, while longer eosin staining will give pinkish red corpuscles. The specimens were dried in air and mounted in balsam.

Discussion.

Dr. Ewing: I have seen the specimens now exhibited and have had an opportunity of examining them, but I am unable to say whether they are parasites or not, though from their appearance I am inclined to think they are.

PARATYPHOID INFECTIONS.

WARREN COLEMAN, M.D. AND B. H. BUXTON, M.D.

Gilbert proposed the terms "paratyphoid" and "paracolon" in 1893, to designate the intermediates of the typhoid-colon group of bacilli. Durham calls the intermediates the "Gaertner-group." The group includes Bacillus enteritidis, Bacillus psittacosis, Bacillus paratyphosus, Bacillus choleræ suis, and some others.

The intermediates are pathogenic for man; Bacillus enteritidis induces epidemics of meat poisoning, Bacillus psittacosis a peculiar epidemic broncho-pneumonia with typhoid symptoms, and Bacillus paratyphosus a disease closely similar to typhoid fever.

Attention is confined in our paper to paratyphoid fever. Thirteen cases have been reported in whose blood, stools, urine, or complicating inflammatory processes paratyphoid bacilli have been found. Four cases have been reported in which the diagnosis was made by the serum reactions. We report a fourteenth case, clinically identical with typhoid fever, in blood of which a paratyphoid bacillus was found.

An analysis of the symptoms of the reported cases shows that the disease closely resembles typhoid fever. All the cases were regarded as such until a bacteriological examination revealed their true nature. None of the cases gave the Widal reaction, and it is thought that other cases of clinical typhoid fever which have failed to give the reaction may have been paratyphoid infections.

Bacteriologically, the bacillus isolated from the case closely resembled Bacillus typhosus in many biological characters, but produced gas in glucose media.

This case shall be reported in full later.

Discussion.

Dr. N. E. Brill: I would like to say a few words in reference to the clinical aspect of the subject. About five years ago I called the attention of the medical profession to a group of cases which clinically bore some resemblance to typhoid fever, but in which the Widal reaction remained persistently absent throughout the disease and subsequent convalescence. There could be no doubt about the absence of the Widal reaction as examinations were made every day in each case, not only during the stay in the hospital, but after they had left. At that time I was impressed with the specifity of the Widal reaction, and on that account I attempted so far as my resources permitted and the facilities of the laboratory at Mount Sinai Hospital allowed, to determine the cause of the infection in the seventeen cases of this class which came under my observation. It should be remembered that at that period, outside of Elsner's and Hiss' media, no differential method of culturing the Eberth bacillus had been suggested, nor had any attempts been made to differentiate the organisms whose biological situation was intermediate between the typhoid bacillus at the one side and the colon bacillus at the other. The bacteriological work, therefore, while it was serious, could not be taken when viewed in the light of present methods as very reliable. It was sufficient, however, to prove that in the feces and in the blood withdrawn from the spleen —a procedure which I would not now countenance—of the cases reported the typhoid bacillus was absent. A bacillus answering to the ordinary tests of the colon bacillus was isolated. At that time, bearing in mind the specific nature of the Widal test, we tried the reaction of the blood in each of the seventeen cases with a culture of the isolated bacillus, but failed to get a reaction. In two of the cases the effect of the blood of the patients upon a culture of the bacillus obtained from each patient respectively failed to give a reaction. This shows that at the time I appreciated the fact that some other organism than the one isolated was the offending and disease-producing organism. The bacteriological work was finished before I read of Widal's observation of a paracolon bacillus from an œsophageal abscess which had casually come into the hospital in Paris. There was no clinical observation in the case of Widal's, as I remember it.

When I presented my paper based on the examination of these seventeen cases I insisted upon the view that these patients did not suffer from typhoid fever, but from some other infection. One of the strongest factors which induced me to form this belief was the fact that a nurse at the training school at the hospital had had an undoubted case of typhoid, six months before, with a Widal reaction, and became ill again with an infection which clinically was similar to the first but in which the Widal reaction was persistently absent, and in blood aspirated from the spleen no typhoid bacilli could be found, though there was found a bacillus which I at that time regarded as the ordinary colon bacillus.

My view of the presence of another than the typhoid infection was bitterly assailed, and in speaking of the cases with Dr. Osler, he regarded them as typhoid. Shortly afterwards, Norman B. Gwyn of Johns Hopkins, published a case which was similar to those I had previously reported and from whose blood he had isolated a paracolon bacillus. From that time on (from 1898) I insisted at various societies that my cases were not cases that should be classified under the head of typhoid fever, but that they were most probably the result of a disease due to a paracolon infection. The expression of this view has always called forth opposition, and it was only three months ago that the worthy President of this Society, Dr. Ewing, fiercely assailed it on an occasion when typhoid fever was the subject for discussion at a meeting of the New York County Medical Association. At this meeting I again called attention to the fact that some cases reported as typhoid were not typhoid, but might probably be a disease due to a paracolon, or as the reader of the evening called it following Schotmüller, a paratyphoid infection.

In conclusion, I wish to say that clinically, as I showed in my paper nearly five years ago, these cases can be readily differentiated from typhoid, notwithstanding they so closely resemble that disease. Under all circumstances I contend that I have the right to claim priority for myself in clinically calling the attention of the medical world to the possibility of some cases like my own being not a typhoid but a paratyphoid infection, and in accurately describing these cases.

I do not believe that my reported cases were of a solitary epidemic, because since then, and almost every summer, I have met identical cases, and at this moment I have two cases in the hospital with a most probable paratyphoid infection.

Dr. Libman: I wish to draw attention to a few points to show that the subject is by no means a simple one. On a previous occasion when this matter was under discussion, Dr. Meltzer threw out the suggestion that in some of the cases referred to there might have existed a mixed infection; cases in which an infection by a paracolon bacillus was followed by an infection by the typhoid bacillus. In connection with this I wish to call attention to the case I am studying in which it is very probable that the reverse occurred. In this case a paracolon bacillus was isolated from the blood twice during life and from the organs post-mortem. Typhoid bacilli could not be found, but the blood of the patient a few days before death gave a positive reaction with the typhoid bacillus in a dilution of 1–250. The blood gave a thread reaction, so-called, with the paracolon bacillus in dilution of 1–20. I would draw attention to the necessity of watching for this reaction at an interval of from four to twenty-four hours after making the test. I think it is highly probable that in these cases the infection with the paracolon bacillus is of a secondary character.

Dr. Ewing: Walker's experiments in Tavel's laboratory would lead one to believe that unless sera are extremely potent and the dilutions very high, they fail to produce the desired results. Dr. Coleman has spoken of the necessity of using different cultures in the differentiation of typhoid species. I have tried for two months to get the Widal reaction in supposed cases of paratyphoid, but have met with no success which would lead me to the routine use of multiple cultures. I believe that the ideas on this subject would be better correlated if we retain the term typhoid in all these cases, and at the same time recognize that the bacterial causes of typhoid fever are more diverse than has heretofore been supposed.

Dr. M. Manges: I would like to comment upon the distinctive character of these cases of paratyphoid, chief among which seem to be the rather abrupt onset and termination, the short cause, the absence of abdominal symptoms, and the failure to respond to the Widal reaction. I believe that a further study of the subject will lead to a simplification and perhaps entire change of some of our views in regard to typhoid. I do not think that these cases of paratyphoid infections can be distinguished clinically from true typhoid, as Dr. Brill seems to think

I regard the differential diagnosis as very difficult, at least in my own experiences.

Dr. Charles Norris: I consider that the term paratyphoid is a very poor one to use, and that in adopting it we are making the same mistake as our forefathers did when they first used the term "typhoid fever". The group of bacilli giving rise to diseases resembling typhoid is a very large one, including many varieties, from the hog cholera bacillus downwards; but it is becoming the custom to recognize nothing as typhoid except that which has the specific bacillus known as the cause of the disease and bearing the same name. Further confusion has been caused by two or three different names having been given to probably the same micro-organism.

Dr. S. J. Meltzer: In some respects I am perhaps responsible for the name "paratyphoid" which has been applied to these cases, and I think that at present it is the most appropriate term that could be used, inasmuch as the clinical symptoms resemble those of typhoid, and one can not very well employ the word "paracolon" because there is no class of diseases known as colon diseases.

Dr. Coleman: I wish to repeat that the reason for calling the cases paratyphoid was that they bore such a strong clinical resemblance to typhoid.

A DEMONSTRATION OF THE TECHNIQUE OF THE DETERMINATION OF THE FREEZING POINT OF BODY FLUIDS BY MEANS OF THE BECKMANN APPARATUS.

F. C. WOOD, M.D.

This apparatus consists of a thermometer with a very finely divided scale and two small glass vessels, one of which acts as container for the solution to be tested, the other as an air jacket to equalize the action of the freezing mixture in which the vessels and the thermometer are placed. The thermometer can be read to a thousandth of a degree if a lens is used and must be adjusted and tested before use by freezing some distilled water, thus determining the zero of the instrument. While the cooling of the fluid is taking place, constant stirring must be done with a small platinum wire which extends down through one of the corks closing the inner freezing vessel, which contains the fluid to be tested. The whole apparatus is placed in a large jar with a mixture of ice and salt, containing enough salt to reduce the temperature about one to two degrees below zero Centigrade. This will necessitate only a moderate amount of salt, and the mixture should contain a good deal of water. The whole is to be wrapped in a thick felt cover to prevent sudden changes of temperature. As the liquid in the freezing chamber cools the mercury will be noticed to sink gradually below the freezing point of the fluid; and if now rapid stirring be begun and especially if the stirrer be allowed to strike the bottom of the vessel, small particles of ice will be formed and will be whirled up through the rest of the fluid, at which instant the mercury will be observed to rise rapidly for a few tenths of a degree and finally remain constant at a given point, which point cannot be altered by stirring. This is the desired freezing point of the liquid.

The rise of temperature is due to the fact that the fluid has become undercooled; that is, has been cooled below its freezing point. When the ice separates, the latent heat of the water is set free and the temperature of the mixtures rises in the case of pure water to zero C.; in the case of one of the animal fluids to the freezing point of that fluid. These observations must be repeated three or four times, and the average taken of the readings. They should not vary more than a few thousandths of a degree from each other.

The determination of the freezing point of distilled water, in other words, the zero of the instrument, must be made every day, for when the mercury rises to room temperature point the glass of the bulb takes a set which prevents the mercury returning accurately to zero when it is suddenly cooled. The accurate zero is only reached after the thermometer has been cooled for some time. In making a series of observations, it is well to keep the thermometer in an ice-box, so that the zero will not vary, in which case it will not be necessary to adjust the zero every day.

The under-cooling should be limited to about three or four tenths of a degree, and if, as is frequently the case, the fluid refuses to form ice at this temperature, it is necessary to stir the mixture by raising the stirrer up to a level with the small side tube with which the freezing tubes are equipped, and then to touch this stirrer with a small particle of ice or a frozen portion of the substance which is being tested. This causes a small quantity of ice to form on the platinum ring of the stirrer and when the latter is dropped again into the fluid, formation of ice will immediately begin, and the mercury will rise to the freezing point desired. The apparatus may be simplified somewhat for clinical purposes by using instead of a freezing mixture of salt and ice, a closed vessel containing ether through which is drawn a current of air by means of a small water pump. The rapid bubbling of the air causes evaporation of the water and a rapid reduction of the temperature of the freezing vessel containing it.

With this apparatus it is often possible to make a determination in ten to fifteen minutes. With the Beckmann apparatus, owing to the large size of the bulb of the thermometer and the necessity for its adjustment, it will usually take about two hours for each determination. Time may be saved by using a thermometer with a fixed zero instead of the Beckmann thermometer, in which case the mercury bulb can be made much smaller; but the results obtained are as a rule not as accurate as those furnished by the original form of the Beckmann apparatus.

The thermometers should be standardized by comparison with some known instrument, or what is better, carry a certificate of the Reichs-Anstalt that they are accurate.

The importance of the determination of the freezing point of animal fluids is that it gives a physical method of determining with very considerable exactness the molecular content of the fluid and with it the osmotic pressure which that fluid exerts. The basis of the whole matter was originally observed by the English physician, Blagden, in 1788. He discovered that the freezing point of a solution was lower than that of a pure solvent and that this lowering of the freezing point was proportional to the amount of substance contained in solution. This observation remained unused until within the last few years, when with the development of physical chemistry, it was found that the molecules of a substance dissolved in a fluid acted just as the molecules of a gas act, and that the osmotic pressure when measured directly was proportional to the amount of substance dissolved in the fluid, just as the pressure of gas is proportionate to the number of molecules contained in a given volume.

These facts are true without further consideration when the solution is of a certain nature, such as benzol, but when we come to determine the osmotic pressure of an aqueous fluid, we find that the proportion between the quantity of substance present and the pressure is not exactly the same. This has led to the further hypothesis that when substances are dissolved in water they undergo a partial decomposition into ions, and that these ions act as free and independent molecules, thereby raising the osmotic pressure of the fluid proportionally. This occurs only in dilute solutions, such as are found in the human body. Inasmuch as the direct measurement of osmotic pressure is very time-consuming and very difficult, the freezing point method has found general application in the determination of a number of considerations. It has been found, for example, that in cases where the permeability of the kidney is in any way injured—and the best instance of this is seen in a chronic nephritis—that the number of molecules in the blood is increased owing to this inability of the kidney to excrete the molecules into urine. This molecular retention in the blood causes only very slight changes when measured in the ordinary way by specific gravity, but gives a marked increase in the lowering of the freezing point as compared with normal blood. If we take the normal freezing point of the blood as .56° C., we find that the presence of a marked obstruction of the kidney will often raise this point to .71° or .72° C., and thus indicate a retention of molecules in the blood. The method does not give us any clue as to the nature of the substance retained but this may be obtained by chemical analysis. It, however, does give us a measure of the amount of substance retained and as it is fairly easy to obtain, while chemical analysis requires days for its results, it has been hoped that this method would afford us a rapid and accurate means of diagnosing inefficiency in the excretory power of the kidney. This hope has been partially realized, notably by Koranyi, who has found that not only in experimental nephritis in animals, but in nephritis in human beings, this rise in the molecular content of the blood could be sufficiently demonstrated. Unfortunately for the practical application of this method, there are many complicating circumstances, the chief one being the fact that cyanosis increases the freezing point of the blood, just as does a kidney inefficiency. The method, therefore, does not give us true results when cyanosis is present. A great deal of work has been done in the determination of the freezing point of urine in hope that this might give us a clude to the kidney work, but at present no definite conclusions have been reached. Caspar and Richter have shown, however, that if we collect the secretions of the kidneys separately by catheterization of the ureter, and then make a determination of the freezing point of the urine received from each kidney, we can obtain a proportional value which gives us the relative capacity of each organ. If then we suspect from the reduction of the freezing point in the blood below .56° C., that the kidneys are inefficient, by obtaining the freezing point of the urine from each kidney we can determine the efficiency of each, and in this way discover which kidney is diseased and whether, if one be removed, the other will have sufficient excretory power to handle the products of the bodily metabolism.

An interesting observation of the care necessary to carry out these determinations is shown by work done by Krönig and Fueth, which has recently been published as a criticism of a paper by Veit. The latter obtained different results when he determined the freezing point of the blood of the mother and the new-born child; and the difference was such as to represent a pressure difference between the fœtal blood and that of the mother of five pounds to the square inch. It was difficult to understand how so delicate a partition wall as the chorionic membrane could withstand such a pressure, so Krönig and Fueth undertook a re-examination of the entire subject. After a very careful series of observations they showed that the presence of the blood corpuscles in the fluid to be frozen made no difference in the result. They also determined by a long series of observations, the average error of the thermometer used. This error between two standard instruments was about nine one-thousandths of a degree. Then allowing for this error a series of freezing point determinations were made with the blood from the mother and the child, and they were found to be the same within the limits of error of the instrument.

CONGENITAL STENOSIS OF THE AORTA AT THE ISTHMUS.

E. LIBMAN, M.D.

This specimen is a striking example of a type of congenital cardiac lesion which is compatible with long life. According to Vierordt, there are about one hundred and thirty cases of the malformation on record; it being second in frequency to pulmonary stenosis. The average duration of life is thirty-four years; one case lived to be ninety-two years old.

The stenosis usually occurs at the isthmus, the ductus remaining more or less open or being closed. The exact site is at the opening of the ductus, just below or above it. The stenosis may be ring-like or funnel-shaped. All degrees of contraction occur down to complete occlusion (fourteen cases of occlusion are recorded).

The collateral circulation is carried on mainly by branches of the subclavian arteries communicating with the intercostal arteries, and with some of the branches of the external iliacs. The development of large anastomosing arteries under the skin of the chest and abdomen is a natural result. The diagnosis can be made in adults rather readily, but hardly in young children, in whom the the large subcutaneous arteries are developed. The diagnostic signs are: hypertrophy of the left ventricle; a systolic murmur heard over any part of the heart, usually loudest at the base or at the apex; the disparity between the pulsations of the arteries of the upper and lower extremities; and the presence of pulsating vessels under the skin of the chest and abdomen in which the wave is from above downwards. This last reservation is made because of the existence of a case published by Türk, in which all the signs of aortic stenosis were found, but the pulsation in the subcutaneous vessels was from below upwards, and the arterial pulsations in the lower extremities were more marked than in the upper. A diagnosis was made of obstruction of the large vessels arising from the arch of the aorta due to specific arterial changes. This was confirmed by the autopsy.

Cyanosis is not a usual symptom in these cases.

The specimen which I have here was obtained at the post-mortem examination of a man, sixty-three years of age, who was admitted on November 1, 1901, into the service of Dr. Rudisch in the Mount Sinai Hospital. The family history was negative. Previous history: For five years he has suffered from dysponoæ and palpitation. No history of syphilis or gonorrhœa. Marked tabacco habit; moderate alcoholic habit.

Present history: For five months he has suffered from dysponœa, palpitation, œdema of the legs, and diminution of the volume of urine. He has been treated at various hospitals without relief. He now coughs and expectorates much muco-purulent material.

As to the status on admission, I shall give only the main points. The finger tips were cyanostic. There was marked general œdema. *Lungs:* Subcrepitant rales over both; friction rales at the right base. *Heart:* Apex-beat, fifth space, two and one-half finger breadths outside the mammillary line (16 cm. from the median line). Left border, 17 cm. from the median line. Right border, 4 cm. to the right of the median line. Systolic murmur at the apex, not transmitted to the left, and heard very well in the fourth space to the left of the sternum. The murmur was not heard in the vessels of the neck. Pulse, 90. Moderate sclerosis of arteries. Liver and spleen enlarged.

The urine was diminished in quantity. On examination it was clear, acid, specific gravity 1,022; 1% of albumen present; hyaline casts.

The subsequent history was no different from that which is usual in cases of disturbed compensation from other causes. The patient died from an intercurrent erysipelas on February first.

On post-mortem examination there was found marked œdema of the entire body. Under the skin of the anterior thoracic and abdominal walls was a mass of varicose arteries varying in size from ⅓ to 1 cm. in diameter. The walls of these arteries were thickened and some were completely occluded. In the anterior mediastinum was an accessory thyroid. The heart weighed 730 grams. The wall of the right ventricle measured 1.2 cm. in thickness. The pulmonary artery was notably dilated. The wall of the left ventricle measured 2.4 cm in diameter.

The aorta at its origin measured 8.5 cm. in circumference; at the origin of the large vessels, 14 cm.; at the isthmus, 6 mm. (in diameter); beyond the isthmus, 9½ cm. in circumference; at the lower part of the thoracic aorta, 6 cm. The abdominal aorta at its upper part measured 5 cm. in circumference; at the lower part, 4.8 cm. The right iliac measured 2.9 cm. in circumference; the left about the same. The innominate artery at its origin measured 14 cm. in circumference; the left carotid, 5 cm.; and the left subclavian, 4 cm.

It will thus be noted that there was a considerable stenosis at the isthmus with dilatation in front of the isthmus and below it. The left carotid and subclavian arteries were dilated to twice their normal size. The arch of the aorta at its origin showed but moderate atheroma, as did also the coronary arteries. Directly in front of the stenosis there was a thick spur of calcareous material, and in the dilatation beyond the stenosis the aorta showed very marked atheroma. The remainder of the aorta and the peripheral vessels showed moderate atheromatous changes.

The spleen was much enlarged, weighing 400 grams; and the liver which presented the changes of chronic congestion with some cirrhosis, weighed four pounds.

As a counterpart to this case, I show here a case of stenosis of the isthmus of the aorta from a child one and a half years old, which died in the service of Dr. Koplik some eighteen months ago.

In this case it will be noted that the isthmus of the aorta is contracted only to about half its normal size, and there were no atheromatous changes present. There was no subcutaneous collateral arterial circulation yet evident.

Discussion.

Dr. Connor: Is dilatation below the stenosis at all common? It seems a strange and inexplicable condition.

Dr. Libman: In these cases various conditions of the aorta below the stenosis had been found. It has either been normal, stenosed, or, as in this instance, dilated. I imagine that the cause of the dilatation was the effort of the blood to get back into the arch of the aorta. It seems probable that little or no blood could be propelled into the thoracic aorta and therefore the collateral circulation through the intercostal arteries might be carrying enough blood into the thoracic aorta to dilate it. To corroborate this point of view I should like to point out that the intercostal arteries which arose from the dilated portion were much larger than those arising from the lower part of the thoracic aorta and from the abdominal aorta. The valvular arrangement on the distal side of the stenosis indicates distinctly that the stenosis was not due to cicatrization of atheromatous ulcers, a condition which one might be expected to exclude in such a case.

A CASE OF ANTHRAX.

L. T. LEWALD, M.D.

The patient, an Italian, fifty-eight years of age, had been employed as a stevedore, and in this capacity had been engaged in unloading sheep's hides. He was admitted to the Erysipelas Pavilion, Bellevue Hospital, on March 1, 1902. Three days before he had noticed a small pimple in the submaxillary region. On the following day he was seriously ill and unable to go to work. On the third day he was admitted to the hospital. His temperature then was 102°, and it rose rapidly to 108°. Afterwards it dropped to subnormal; but the man continued to grow worse and died on the day following his admission. When he was admitted the only lesion which was noticed was a small ulcerated area about half an inch in diameter with a dark eschar in the center and surrounded by a number of small blebs and a diffuse redness. There was considerable oedema of the face and neck; and this spread rapidly to the chest and also to the forehead to such an extent in the latter direction that it completely closed the right eye. Afterwards signs of cyanosis developed and death occurred about twenty-four hours after the man had been admitted. A smear was made from the wound in the neck a few hours before death, and the examination made at the laboratory confirmed the diagnosis of anthrax. The antopsy was obtained forty-eight hours later and showed the following conditions: The body was well nourished and rigor mortis marked. On the right side of the neck, in the submaxillary region, there was a small ulcer covered by a slight scab. In the surrounding tissue there were a number of small blebs containing a slightly serous fluid. There was a marked swelling and oedema of the face and chest. The brain showed intense congestion. The heart was of normal size. The left ventricle was contracted, the right ventricle dilated. The lungs were congested and the liver showed remains of a few old adhesions. The kidneys showed a slight degree of chronic nephritis. The spleen and pancreas were normal. The stomach was dilated and the mucous membrane showed signs of chronic gastritis. The epiglottis was markedly oedematous, in fact, sufficiently so to account for death. Smears taken from the left ventricle of the heart showed a considerable number of large bacilli of the anthrax type, and the culture from this source developed anthrax. Cultures from the spleen also showed anthrax bacilli, as did likewise cultures and microscopic examinations of stained sections of the liver. There was very slight parenchymatous degeneration of the liver and of the kidneys on microscopic examination. The lungs and spleen showed acute hyperaemia. The subcutaneous tissue surrounding the area of infection was almost necrotic.

The points of special interest in the case are: The mode of infection, apparently derived directly from the handling of hides; the widespread oedema, starting in the immediate vicinity of the wound of entrance and resulting by direct extension in oedema of the larynx and death; the absence of acute hyperplasia of the spleen or other ordinary evidence of a severe septicaemia, although anthrax bacilli were found in the liver and spleen at the autopsy.

Discussion.

DR. CONNER: In my experience anthrax is much less infrequent in this city than was commonly supposed; and this seems to be just the type of men among whom the disease develops, longshoremen whose duty it is to handle hides. Within the last three or four years, four or five cases have come into the dispensary of the Hudson Street Hospital. Singularly good results have been obtained from early radical excision. As the prognosis depends largely on early recognition of the disease, it is well to emphasize the fact that cases of the kind are not uncommon and that they are likely to be met with in the dispensary rather than in the hospital ward.

DR. EWING: Was there any bacteriological examination made of the blood?

DR. LEWALD: No such examination was made during life?

DR. EWING: It is desirable that the blood should be tested with the view of ascertaining whether it was a form of true septicæmia. It is all the more important because to determine the presence or absence of the bacilli in the blood since various conflicting reports which had recently been published as to their presence in the general circulation in cases of human infection.

A CASE OF HODGKIN'S DISEASE.

E. L. DOW, M.D.

This case is one which was observed in the wards of Bellevue Hospital, and which was regarded as a typical case of Hodgkin's disease remarkable for the unusual ulceration of the tonsils.

The history of the patient was as follows: He was a laborer, forty-five years old, had had no disease except pneumonia some eighteen years previous to his admission. No history of syphilis. For the past five years, he had not been as strong as usual nor able to carry out his regular work. The year before his admission to the hospital he noticed a small swelling under the angle of the right jaw. This slowly increased in size, and seven months latter he noticed other hard swellings on the left side of the neck and in both groins. With the appearance of these groin tumors he also began to notice that he had difficulty in breathing. The tumors were painless. For the past seven months the tumors have been rapidly increasing in size, and are now very large, filling up the entire lateral aspect of the neck, and forming large masses in the groin. Swallowing is difficult and painful. Expectoration has been at times blood-tinged and mucopurulent. He had not lost flesh at the time of his admission to the hospital. When admitted the tumors were found to be circumscribed, irregularly spherical masses quite uniformly firm and elastic without any evidence of suppuration. The skin was freely movable over the tumors. In the neck they were situated immediately under the lower jaw on the floor of the mouth and below the ears, pushing the chin up so that opening of the mouth was limited. In each groin there was a similar character with discrete nodules the size of a large fist. In the axillæ were similar swellings the size of an English walnut. Indistinct masses could be palpated through the abdominal wall in the iliac and lumbar regions. The patient appeared fairly well nourished but anæmic. The dysponoea was extreme and the breathing stridulous. The jaws could not be separated sufficiently for a pharyngeal examination. The heart, lungs, liver, and spleen showed no marked abnormalities. On admission his temperature was 101.6°; pulse, 120; respiration, 30.

During his stay in the hospital he had an irregular temperature varying from 100° to 103°. Examination of his blood after admission revealed 3,600,000 red cells and 2,900 whites to the ccm. The number of leukocytes remained low until his death. The urine was normal. Sputum examination showed no tubercle bacilli. During his stay in the hospital, the dysponœa and difficulty in swallowing became so great that he took no food voluntarily. Death due to pulmonary œdema.

The autopsy, six hours after death, showed a fairly well nourished body, slight œdema of the legs. In the cervical, inguinal, iliac, lumbar, and mesenteric regions were found the tumors previously mentioned. The secondary and tertiary lymph nodes were not involved. Those in inguinal regions each weighed 10 oz. They were composed of numerous lymph nodes enlarged and bound tightly together. Everywhere the nodes were discrete. In the iliac chain they showed little fibrous structure. No evidence of suppuration existed, though some of the nodes broke down under pressure. The anterior mediastium contained a few large lymph nodes; the posterior contained many nodes the size of English walnuts which extended round the roots of each lung, forming masses the size of a fist. Bronchi, trachea, and larynx were intensely congested. The tonsils were deeply ulcerated and hyperplastic. The entire pharyngeal lymphoid tissue was markedly hyperplastic. Chronic changes were found in the kidney. The intestines showed hyperplasia of Peyer's patches and solitary lymph nodes. One Peyser's patch projected a centimetre into the lumen of the intestine, looking very much like a small mushroom. The surface was ulcerated and there was a post-mortem invagination of this portion of the intestine.

Microscopic examination of the ulcerated tonsils and lymph nodes revealed only round cell growth with hyperplasia in all but the iliac, lumbar and mesenteric nodes. There was no evidence of tuberculosis.

The deep ulceration of the tonsils apparently occurs more frequently in those cases running an acute course. A number of observers have noted such a condition in connection with acute inflammations of the throat.

Discussion.

Dr. Wood: In some of the recent text-books it is stated that the lymphocytes in Hodgkin's disease are relatively increased while in cases of tuberculosis simulating Hodgkin's disease no such increase is present. In the cases of Hodgkin's disease, however, which I have been able to examine no such relative lymphocytosis was found. I wish to know if Dr. Dow has noticed this point in his case.

Dr. Dow: I have not.

Dr. Field: In view of the recent discoveries in regard to the pathology of Hodgkin's disease it is important that all such cases should be put through a careful examination for tubercle bacilli.

Dr. Ewing: I would like to add not only for the tubercle bacillus but for other bacteria as well.

Dr. Dow: There was no evidence of tuberle bacilli in the tonsils nor in the lymph nodes. I would like some expression of opinion from the members of the Society as to whether they consider the ulceration of the tonsils a primary or secondary condition. If secondary, why should it occur in the tissues of the tonsils rather than in the hyperplastic lymph nodes?

DEMONSTRATION OF HAEMOLYSIS.

F. C. WOOD, M.D.

The specimen to which I wish to call your attention are those which illustrate the action of foreign sera on corpuscles of different animals. I have selected rabbit's blood and dog's serum to show their mutual interactions.

If we add to rabbit's red blood corpuscles, suspended in physiological salt solution, a small amount of dog serum, the hæmoglobin of the rabbit corpuscles will be extracted and dissolved in the fluid. The same is true if use bullock's serum and rabbit's corpusles. This reaction may be prevented by heating the serum to 58°C., for half an hour. This heated serum will then not cause any laking of the corpuscles. The laking action may be restored by the addition of fresh serum from the same animal from which the corpuscles were removed. For instance, if we treat rabbit's corpuscles with bullock's serum which has been heated there will be no reaction. If, however, we add a small quantity of fresh rabbit serum to the mixture, the hæmoglobin will be extracted. This is evidently not due to any action of the rabbit serum, for such serum is isotonic to its own corpuscles, but is due to the addition of a certain complementary body which enables the altered bullock serum to again lake the red cells by a process which is not as yet fully understood.

CARCINOMA OF THE PANCREAS.

A. E. THAYER, M.D.

The clinical history of this case dates from five weeks before the patient was admitted to the hospital. At that time he began to have severe pains in the lumbar region which radiated forward into the abdomen, were partly relieved by pressure, and which lasted half a day. Such attacks occured at intervals until admission. He vomited at times, but there was no blood in the vomit. His strength and flesh had steadily diminished and for about three days he had been jaundiced. His feces had been formed and yellow.

On admission the patient was poorly nourished; respiration was wholly thoracic; the abdomen was tense, retracted, and generally tender on palpation; and in the epigastrium and reaching into each hypochondrium there was a prominent mass of irregular outline. Neither liver nor spleen could be made out. The urine contained no albumin nor sugar, but was deeply bile-tinged. The entire surface was deeply jaundiced.

The patient's temperature varied between 99° and 101°; respiration about 28 to 30, and pulse 120 to 130, while he was in the hospital. An exploratory operation was performed, and from that time he sank, having diarrhœa, and vomiting a dark fluid till he died from exhaustion about three weeks after admission.

At the autopsy there was found a large mass in the pancreas, the older portions about midway of its length showing cystic softening and involving the spleen and the left adrenal. The lymph nodes about the gland were generally involved. On the upper posterior aspect of the liver there was a single direct metastasis, which had nearly penetrated a large branch of the hepatic vein. The colon contained bluish-gray feces; the gall-bladder was a little distended. There was no dilatation of the stomach nor contraction of the duodenum. On microscopic examination the tumor was found to be adenocarcinoma. No trace of pancreatic tissue was left, and almost no splenic.

I wish also to present a case of suppurative cholangitis, due to biliary calculi impacted in the common duct. In this case there is no clinical history. The patient, a Russian of about forty-five years, was intensely jaundiced and much emaciated. Post-mortem six gall-stones were found impacted in the common bile duct, lying in a collection of pus. All the larger branches of the bile ducts through the liver contained pus and small grains of black pigment; and in the left lobe there were several abscesses, about 3 to 5 cm. in diameter. The gall-bladder was much distended, contained grayish-green, thickened mucous fluid and grains of pigment, and from its inner wall there grew a small soft fibroma. There was no distension of the pancreatic duct, no interstitial pancreatitis nor fat necrosis. There was complete hyperplasia of the left kidney.

The two cases are of interest as showing how little reliance can be placed in Courvoiser's law, so-called: that with bile stones the gall-bladder is small, and with malignant disease of the common duct it is large. A number of recent cases demonstrate that this view is untrustworthy. The relation between occlusion of the common bile duct and pancreatitis and fat necrosis also appears to be slight from these cases. Further, in each there might have been sugar in the urine, especially in the first case where the pancreatic tissue was wholly replaced by a neoplasm, but, so far as the records show, there was none.

CARCINOMATOUS ULCERATION OF DUODENUM, WITH ABCESSES OF LIVER AND PANCREAS.

JOHN H. LARKIN, M.D.

For several years the Society has been receiving reports on perforating ulcers of the duodenum, but the present case is of exceptional interest because of the complications disclosed by the specimen, although I must apologize for the incompleteness of the history of the case.

The patient was a woman, forty-six years of age, an Icelander, and it was difficult to obtain any facts beyond this, that for about two months she had been ill, simply with pains in the lumbar region. No physician had seen her until two weeks previous to her being admitted to the hospital. At the time of her admission the case was put down as one of ordinary destitution and starvation. Three hours before death, she had a large and copious bloody movement from the bowels, then went into a collapse and died.

At the autopsy an interesting condition of the organs was revealed; but before speaking of this I wish to say a word about the symptoms. At no time, so far as could be ascertained, had there been any abdominal pain or vomiting. At the autopsy I found the body markedly emaciated. There were no evident signs of peritonitis; some clear serum in the abdominal cavity. All the viscera were normal except that they were pale and blanched from loss of blood. The sudden hemorrhage and collapse pointed to an intestinal lesion. I expected to find an abdominal aneurysm with perforation into intestine, but in this I was mistaken. In the stomach there were two pints of clooted blood, but the mucous membrane was perfectly normal. On going down to the duodenum I discovered a large, irregular ulcer, about the size of a dollar, with several small nodules at the periphery. In the center was a large necrotic mass directly through the duodenum, and the adjoining liver tissue was extremely necrotic, making a large abscess cavity filled with pus and recently coagulated blood. In the middle of pancreas was a small metastatic nodule, firm and fibrous. The blood vessels were dissected up and the superior mesenteric vein was found necrotic and leading directly into the abscess cavity. Microscopical examination of sections taken from edge of ulcer in duodenum and mass in pancreas showed adenocarcinoma.

MULTIPLE EMBOLI OF MESENTERIC ARTERIES.

C. PHILLIPS, M.D.

The case is that of a physician, thirty-three years of age. His past history showed that he had always been a well man and had never veneral disease or gout. He gave a vague history of attacks of pain, five years before, in the right inguinal region, lasting two or three days.

The patient was quite alcoholic, drinking beer and whiskey, and an immoderate eater. For three or four nights before the onset of present trouble, the patient had been intoxicated. He awoke in the morning about four o'clock, complaining of severe abdominal pain which was constant and general. He rapidly developed tympanites and the entire abdomen became generally painful on palpation. There was no localize tumefaction or increased resistance to pressure. He had considerable hiccough and vomited a few times, but no blood. It was impossible to get a movement of his bowels by cathartics or high rectal enema. Pulse rate was between 80 and 90 and he had no fever. During the first twenty-four hours, he passed but 8 oz. of bloody urine.

About forty-eight hours after the onset of the symptoms, he was operated upon by Drs. Bull and Coley. The abdominal cavity contained about 1500 c.c. of sero-sanguineous fluid with some flakes of fibrin. The small intestine was much cyanosed, markedly distended with gas, and here and there were small hemorrhages under the peritoneum. The omentum was much swollen and contained also many hemorrhagic food. There was no obstruction of the intestine found. The patient died four hours after the operation, and an autopsy was performed by Dr. Harlow Brooks, to whom I am indebted for the following notes:

On opening the peritoneal cavity about 300 c.c. of creamy pus escapes, and the parietal and visceral layer of the peritoneum is covered with a thin layer of fibrinous pus. The entire gut is distended with gas, particularly the cæcum. The peritoneal capillaries are much injected both on the walls and over the intestines. The omentum is very short and thick and laterally studded with small spherical injected gangrenous nodules, which appear not unlike Delaware grapes. Evidently they represent minute embolisms of the omental vessels. The omentum is much walled together, as from previous disease. The mucosa of the stomach shows evidence of chronic gastritis and numerous old healed ulcerations of small size. The appendix is sharply folded on itself and surrounded by œdematus adipose tissue and old adhesions. It is about 2 cm. long, and has evidently ruptured with complete loss of the distal two-thirds. There are no evidences of recent inflammation.

The mucosa of the small intestine as a whole is much congested but in places is chæmic. There are a few minute emboli of the submucous vessels but more frequent and larger lesions of the same character on the peritoneal surface, resulting in small gangrenous patches.

The mesentery of the lower folds of the ileum shows a very marked congestion with the presence in the small vessels of minute emboli. This condition becomes more frequent in the upper folds of the mesentery where the emboli are larger. The mesenteric vessels as a whole show the most marked evidence of recent endarteritis; while here and there are portions of the intima which are calcified.

The pancreas is riddled with fat infiltration. The calibre of the artery is about that of the axillary with enormously thickened intima. The pancreatic duct is gangrenous in part, apparently from thrombosis of its nutriment artery. There is extensive infiltration of the pancreatic interstitium, apparently inflammatory. The liver is moderately fatty and considerably congested. The kidneys show evidences of acute nephritis with very evident fatty degeneration.

The heart is large and the muscle shows extensive fatty degeneration. The valves are thin but competent. In the right auricle is a preformed clot, evidently of two or three days duration. It is distinctly laminated, very firm, and on the surface it is covered with small granulomatous masses. It is firmly adherent to the superior external wall of the auricle and shows beginning organization. The coronary muscles are much thickened and atheromatous. The aorta is of small calibre but atheromatous throughout. The lungs are congested and show here and there small recent hæmorrhagic infarctions.

Cause of death: Multiple infarction of the pulmonary and mesenteric vessels from thrombosis of the right auricle; this condition occurring in acute alcoholic toxæmia.

No cultures were taken.

ENDOTHELIOMA OF SERUS CAVITIES.

C. W. FIELD, M.D.

The patient, from whom the specimens were taken, was a woman fifty-six years of age, a widow with three children. The history of the case was negative, except that for some time she had a hacking cough and that her stomach had always been weak. She had been losing strength for two years. Pulmonary symptoms afterwards developed, but there was at this time no vomiting or gastric disturbance. The woman was admitted to the Presbyterian Hospital on December 20, 1901, after having been affected by nausea and diarrhoea for three weeks. A physical examination made on January 27th showed a marked adhesion over the whole of the right lung. The patient continued to grow worse and died soon afterwards, having previously vomited a large quantity of bloody serum.

At the autopsy a very thorough examination was made of all the organs and it was found that the pleura was very much thickened, apparently by a tuberculous lesion. On sectioning the thickened mass, however, it was found to be a new growth of alveolar type, probably to be classed with the primary endotheliomata of the serous cavities. There was also found a tumor involving the optic nerves which was of the same morphological type. The only indication of this new growth from a clinical point of view had been headache of which she complained while in the hospital. The exact site of the origin of the new growth was therefore somewhat difficult to assertain, but it seemed probable that the pleural tumor was primary and that of the optic nerve secondary, though the existence of two tumors developing simultaneously was not impossible.

Discussion.

DR. JOHN H. LARKIN: From the microscopical examination it seems to me that the tumor may have been primary in the optic nerve.

COMPLETE DOUBLE URETER ON EACH SIDE, PERVIOUS THROUGHOUT.

T. C. JANEWAY, M.D.

In presenting this specimen of complete double ureter on each side, I need not detain the Society with any lengthy description, as it is simply a very rare anatomical abnormality. In looking over the transactions of the London Pathological Society and Virchow's Archiv, I have found only one exactly similar case, reported by Ewart. Specimens showing ureter double for a portion of its length on one side, and on the other side one normal ureter and one abnormal one emptying into neck of bladder or prostatic urethra, have been encountered by Weigert, Hoffmann, Tangl, and Wood. Double ureter on one side only seems to be a much more more common condition, cases having been reported by Weigert (seven in one year), Thompson, Durham, Kelly, and Voelcher.

This specimen was taken from a middle-aged woman, who died of chronic diffuse nephritis. It shows the separation of the pelvis of the kidney into two distinct cavities, common to all previous cases, but is unusual in that there is no crossing of the ureters, and that the upper ureter in each side opens above the lower in the bladder, the opposite of Wiegert's findings.

TWO CASES OF LYMPHOCYTOSIS SIMULATING LEUKAEMIA.

FRANCIS C. WOOD, M.D.

The first case was that of a child with a tuberculous lesion of the hip, the lymphocytosis disappearing after drainage of the abscess; the second case was a fatal case of anaemia without lesions in the bone-marrow. Studies of the blood showed marked lymphocytosis in both cases.

Discussion.

DR. EWING: These cases are important additions to the scanty knowledge which exists on this subject and shows the importance of examining other things besides the blood before accepting a diagnosis of lymphatic leukaemia. One feature of extreme interest in the second case is its resemblance to pernicious anaemia. At the same time it differs so much from reported cases of pernicious anaemia without bone-marrow changes, that I would hesitate to accept it as such without study of all the antecedents.

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DR. JAMES EWING, *President.*

PERSISTENCE OF VARIETIES OF THE BACILLUS DIPHTHERIÆ AND OF DIPHTHERIA-LIKE BACILLI.

ANNA W. WILLIAMS, M.D.

The investigation may be conveniently grouped into the four following heads:

1. A study of the dipththeria and diphtheria-like bacilli found in a series of clinically typical diphtheria cases at the Hospital for Contagious Diseases; (*a*) serial smears of cultures directly from throats and noses, (*b*) pure cultures isolated from these cultures.

2. A study of the diphtheria and diphtheria-like bacilli found in healthy and diseased throats in a town during an epidemic of diphtheria; (*a*) smears of cultures

directly from throats, (*b*) pure cultures isolated from these cultures.

3. A study of diphtheria and diphtheria-like bacilli found in sore throats during a epidemic of diphtheria at a home for destitute children; (*a*) pure cultures.

4. A study of pure cultures of diphtheria and diphtheria-like bacilli from sources other than those given above; (*a*) on various artificial culture media grown under various conditions, (*b*) in living tissues of guinea-pigs, white rats, and gold finches, (*c*) in symbiosis with other bacteria.

The results obtained from these studies may be summarized as follows:

1. (*a*) In a series of ten cases of clinically typical diphtheria only one variety of the specifically-virulent diphtheria bacillus was obtained from the throat of each case throughout the course of the disease and until suspicious bacilli disappeared; (*b*) from different parts of the same patient only one variety of specifically-virulent diphtheria bacillus was obtained, (*c*) "pseudo" varieties were found no more frequently at the end than at the beginning of the disease, (*d*) pure cultures continued to show characteristics similar to the original cultures for many culture generations.

2. (*a*) Under normal conditions different varieties of diphtheria-like bacilli may be found in the same throat; (*b*) many throats in a single institution may contain many diphtheria-like bacilli with no case of diphtheria resulting; (*c*) there are many distinct varieties of diphtheria-like bacilli all of which in several pure cultures retain the characteristics of the original culture.

3. (*a*) In each case of diphtheria apparently contracted from the same source the same variety of virulent diphtheria bacillus was found; (*b*) this variety remained

the only variety of virulent diphtheria bacilli found until its disappearance; (*c*) no gradations in pseudo types were found, the same type seen in the first examination continued to be present in later ones; (*d*) pure cultures continued to show characteristics similar to the original cultures for many culture generations.

4. (*a*) Some cultures when grown on artificial media show certain changes, but each culture changes in its own way, retaining its distinct individuality. After many culture generations, however, especially when transplantations are made at short intervals, the different varieties of the specifically-virulent diphtheria bacillus tend to approach each other, or rather to run in lines parallel with a common norm; (*b*) no non-virulent morphologically typical bacillus has been made virulent, neither have solidly staining "pseudo" varieties or other atypical varieties been made virulent or morphologically typical.

These studies seem to demonstrate that the morphologically typical diphtheria bacillus is a distinct species from the atypical diphtheria-like bacilli, and so-called "pseudo" forms; and that it has many true morphologic varieties or sub-species which while showing transitory ontogenic variations due to change in environment and life habit have more or less persistent phylogenic characteristics which re-appear when the organism is placed in a previous environment.

Discussion.

Dr. Park: It is really extraordinary how the characteristics of different bacilli are found to persist for long periods when changed from one culture medium to another and then restored to their original medium. I believe that many of the changes reported in the literature on the subject may be attributed to errors of observation. One thing that particularly interested me was the fact, shown by observations at the Willard Parker Hospital, that, whereas, the diphtheria bacilli apparently differed in virulence at different times when tested in bouillon, in reality they only differed in their rate of growth, and were very much alike when tested in ascitic bouillon. The propability is that in the throat they are always very much the same in respect of virulence.

The practical conclusion which we are entitled to draw from the investigation is that when bacilli began by being virulent they remained virulent to the end; and on the other hand when they are not virulent at the start, they do not become so. This being so, it does not seem that there is any use of the physician making repeated tests in any one case with the view of ascertaining the degree of virulence of the bacilli present. Summing up, the observations establish beyond doubt that the bacillus does not change from one type to another. The experiments have been most carefully conducted and I believe that the conclusions arrived at are correct.

SPONGE FOUND IN OPERATION WOUNDS.

EUGENE HODENPYL, M.D.

The specimens and drawings which I exhibit this evening were obtained from two cases in which sponge had been found in operation wounds. These two cases are illustrative of the experience common to pathologists that rare cases are apt to occur in pairs (Binary occurrence of rare cases). These two cases came under my notice within a period of seven days. Regarding the rarity of the condition I might say that I have never met with it before, nor have any of my colleagues in the laboratory seen any similar case. The sections from the specimens were sent to several pathologists, but none except Dr. Welch were willing to hazard a diagnosis. Dr. Welch said that he regarded the peculiar structures as sponge, and based his theory on the recollection of a case of similar kind which he had seen years ago.

When the cases were studied more carefully the identity of the condition and the accuracy of this opinion became apparent.

The first case was that of a man seventy years of age, who suffered from epithelioma of the pharynx. Three and a half months before he had been operated upon from a primary growth. Directly on the site of the operation, embedded in the connective tissue, I came upon these curious masses, two or three in number. They presented solid threads often branching and anastomosing, sometimes presenting a double contour which stained with a large variety of stains. Although "foreign body" was at once suspected, I was thrown off my guard by the fact that the adjacent muscle showed curious degeneration, and it was thought that various phases between the muscle and these curious masses could be traced.

The second case was even more remarkable. The patient was admitted to the hospital with a history of recurrence of epithelioma of the lip. He had been operated on eight years before for a primary growth. The appearance of the sections greatly resembled those of the first case, except as was to be expected the spicules of sponge showed more evidence of absorption. Many of them were surrounded by giant cells.

Discussion.

Dr. Wood: Dr. Hodenpyl's experience has been very valuable to me, for shortly after the examination of the specimens referred to, I had a similar case in St. Luke's Hospital and I should undoubtedly have considered them as some kind of degeneration if I had not heard of these two cases and been instructed by them of the origin of the condition.

PROTEOSOMA-MALARIA IN SPARROWS.

W. N. BERKELEY, M.D.

The specimens which I submit were obtained last September while at work on the subject of malaria in birds. It was easy in Bronx Borough to find English sparrows (passer domesticus) infected with malarial parasites corresponding in all morphological characters with the proteosoma of Labbe. I examined nearly a hundred birds; seventy-five per cent were infected, and ten to fifteen per cent severely infected. The latter while apparently doing well in the open, sickened rapidly in confinement, refusing to eat and sitting with ruffled feathers in a corner of the cage. The temperature of one bird reached 108.8° F., although I will not venture to say that this figure represents an unusually high temperature in birds.

The heart blood of one bird showed many red cells infected with five to seven sporocytes, apparently multiple infections though I have not noticed similar observations in the literature and am not fully able to claim that this particular malaria infection was a proteosoma case. For the rest the stained specimens speak for themselves.

MULTIPLE DIVERTICULA OF THE COLON; FIBROMYOMA OF THE STOMACH.

J. D. CONDIT, M.D.

The specimen was removed from a female, aged seventy, who gave a history of a long standing chronic nephritis with chronic constipation and frequent attacks of bronchitis extending over many years.

The autopsy which was done in the pathological department of St. Luke's Hospital by Dr. Wood, showed an hypertrophy of the heart with atheroma of the coronary vessels of the aorta and the smaller arteries, marked emphysema of the lungs and chronic diffuse nephritis. The stomach and the small intestine were normal. In the colon were numerous small diverticula, the largest of which measured about one and one-half cm. in diameter. These diverticula were arranged in two irregular rows on either side of the mesenteric border and did not average much over one cm. in diameter. They occupied chiefly the walls of the transverse and descending colon, the sigmoid flexure, and the upper portion of the rectum; but there were a few in the ascending colon. They were filled with small hard fecal masses and communicated with the lumen of the gut by a small constricted neck. There seemed to be no connection between these diverticula and the exit of the portal system of the vessels. No enterliths were found in the diverticula.

The microscopical examination of the diverticula showed that the walls contained the normal coats of the colon. The mucous membrane was somewhat flattened out by pressure; the peritoneal coat was normal. The submucosa was very thin and the muscularis could be seen to still cover the wall of the diverticulum; but was reduced to a very thin layer. The mucosa and submucosa were infiltrated with leucocytes, and showed a moderate amount of chronic inflammation. The presence of the muscular coat in the diverticule may be explained by the fact that the protusions from the wall of the coat were still small, and that atrophy of the muscularis had not yet taken place, as is seen in larger diverticula which measure between three and five cm. in diameter. Such diverticula have been recently shown before the Pathological Society by Dr. Hodenpyl, and in his case the muscularis had disappeared.

Hensemann has shown that the diverticula of the small intestine appear chiefly at the site of exit of the intestinal veins from the gut, close to the mesenteric attachment, and that they usually contain no muscular coat but are hernia of the mucous membrane. In the colon, however, Edel has shown that diverticula are true pouches at first, and that later the muscularis atrophies. They occur chiefly in the aged and in cachectic individuals, associated with atrophy of the muscular coat and extension of the gut with gas or feces.

The second specimen which I present was an accidental find at autopsy of a female, aged sixty, whose death was due to carcinoma of the uterus with involvement of the rectum and bladder. On the anterior wall of the stomach near the pylorus was a small oval tumor, two by one by one and a half cm., with a smooth surface and sessile base. The tumor was very hard and was adherent to the mucous membrane, but protuded on the outer surface of the stomach. When cut across the tumor was very dense with a capsule which contained the remains of the muscular coat and submucosa.

Microscopical examination of the tumor showed it to be composed of irregularly interlacing bundles of fibrous tissue and smooth muscle surrounded by a capsule of connective tissue on the inner surface, and externally blending with the muscularis of the stomach wall. On the portion of the tumor nearest the mucosa there was a moderate amount of inflammation.

These fibromyomata of the stomach wall are rather infrequent. In 1898, Steiner was able to collect only about fifty-six cases of myomata of the gastro-intestinal tract, seventeen of these being in the stomach wall. They are most frequently situated the lumen, but may be contained in the wall or on the external surface, or finally attached to the stomach by a pedicle. They may be oval and smooth, or irregular and lobular in form. Those containing much connective tissue may show softened areas and small cysts filled with clear fluid or blood. In a few cases these cysts have become infected from the bowels and have discharged their contents into the peritoneum with resulting general peritonitis. In a few cases, malignant change of the myomatous tissue is described with formation of metastases in neighboring lymph nodes; but as a rule these tumors are benign and are discovered only accidently or at autopsy.

FALSE DIVERTICULA OF THE SIGMOID FLEXURE; ANEURYSMAL DILATATION ON THE DUCTUS ARTERIOSUS IN A MALE INFANT; SPECIMEN OF CONGLOMERATE TUBERCLES OF THE LIVER.

OTTO H. SCHULTZE, M.D.

The specimen of false diverticula of the sigmoid was obtained from a case which was complicated with fecal abscess and general septic peritonitis, followed by purulent meningitis and lobar pneumonia. It was removed at autopsy from a man about forty years of age. One of the many false diverticula which contained hard fecal masses, through ulceration and subsequent infection, had given rise to an abscess between the sigmoid and left iliac fossa, which had then ruptured into the peritoneal cavity. No clinical history was obtainable. This condition may account for some cases of perisigmoiditis, or cases running a course resembling that of appendicitis, the symptoms being referable to the left instead of the right side.

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The second specimen was obtained from the body of a male infant which was found in a school sink. There were no marks of violence. The ductus arteriosus was dilated and filled with recently clotted blood. Its pulmonary end was closed; its aortic end open and about 7 m.m. in diameter. The duct was 2 cm. in length and over 1 cm. in width, thus presenting the condition of a large sacculated aneurysm in the anterior mediastium, bounded on the left side by the left lung, on the right side by the left auricle, coming in relation anteriorly with the left phrenic nerve and posteriorly with the left pneumogastric nerve. Ecchymoses were found on the pleura, pericardium, and pericranium. No foreign material was found in larynx, trachea, or bronchi. The blood was fluid except the recent clot found in the ductus arteriosus. The condition pointed to asphyxia, yet the positive diagnosis of asphyxia by submersion could not be made. It is by no means uncommon, in New York at least, to find that infants whose bodies are found under circumstances arousing suspicion as above may nevertheless have died from natural causes; since many poor and ignorant inhabitants of large cities are not aware that the authorities will bury their dead. It is an open question in this case as to what effect the condition described may have had in causing death by pressure upon the pneumogastric or phrenic nerves. The size of dilated ductus compared with the size of the anterior mediastium of a three weeks old infant is a matter of some importance.

The liver specimen which I present contained besides many miliary tubercules a large number of conglomerate tubercles, varying in size from 0.5 to 1.5 cm. in diameter whose centers were fluid and bile stained, whose margins were cheesy and surrounded by connective tissue, presenting under the microscope bile pigment and amorphous ditritus in the center; then an area of coagulation necrosis in which miliary tubercles could be faintly made out, and finally tubercle tissue and granulated tissue, in many advanced to the formation of fibrous connective tissue. The subject, a male, eighteen years of age, had a most extensive chronic tuberculous bronchopneumonia, with large cavities, from one of which a hemorrhage had taken place which was the immediate cause of death. The extent of tuberculous inflammation in this subject was most remarkable: the larynx, spleen, almost the entire intestinal tract, peritoneum, bronchial and retro-peritoneal lymph nodes were affected. Large conglomerate tubercles were found in the spleen and throughout the peritoneum. It seems less probable that these so-called bile ducts tubercles originate from an infection of the bile ducts than from an erosion or inclusion of the ducts by the process of tuberculous inflammation in the periportal connective tissue.

A SPECIMEN OF RHABDOMYOMA OF THE TESTIS; A SPECIMEN OF MYOMA OF THE SMALL INTESTINE.

F. C. WOOD, M.D.

The history of the case is that of a young man of eighteen, who had been rather feeble in his youth but had had no diseases except the exanthemata of childhood. Three months before admission he noticed a swelling in the right testicle. The tumor grew rapidly to the size of a fist, but was not painful and but slightly tender in the softened areas. When the patient was examined it was found that the tumor had replaced the testicle on the right side and was freely movable in the scrotum. On palpation there were found to be hard and soft area in the tumor. The softer areas seemed in many cases small cysts. The tumor was removed without difficulty, and the patient was discharged, cured.

The tumor when hardened measured eleven by eight by seven cm.. It had completely replaced the testicle, but had not extended beyond the tunica albuginea. The remains of the testicle and epididymis were still to be found near the periphery of the tumor, apparently pushed aside by the new growth. The cut surface showed many cysts, the largest ones being between one and two cm. in diameter. There were also areas of about the same size of yellow opaque tissue evidently very cellular. A few very small nodules of cartilage could be seen scattered through the cut section. Microscopical examination showed that the tumor was largely made up of loose connective tissue stroma filled in many places with a very large amount of striated muscle fibers showing the spindle and spherical forms which are so often seen in embryonic muscle fibers. In only a moderate number of the fibers could striations be made out, but the staining reactions and the arrangement of the nuclei left no question that many of the smaller round cells were muscle cells not cut transversely, but remaining undeveloped. The connective tissue stroma also showed an embryonic type, very often cellular and softened, with occasional areas of mucous degeneration.

Occasionally the section showed areas of cartilage. In other portions there were epithelial tubules remaining, such as are often found in the teratomata of the testicle. In fact, this tumor might well be classed as a teratoma with excessive development of striated muscle. It does not belong to the group of pure myoma of the testicle of which about six cases have been collected from the literature.

I have also to report a case of myoma of the small intestine. This tumor was an accidental find in the course of a ventrofixation of the uterus. It was attached to the small intestine, a loop of which prolapsed during operation. This loop was evidently a portion of the lower ileum, but the exact distance from the cecum to the tumor was not made out. The mass was a lobular, dark, fibrous tumor attached by a short pedicle to the intestinal wall. It was quite vascular on its surface. The mucous membrane of the intestine were incised around the base of the pedicle and the tumor thus removed.

When hardened it measured four and one-half by three and one-half by three cm. The surface was quite sharply lobular and still showed deep blood staining. A cross section of the tumor showed that it was vascular and also contained a number of cysts. The mucous membrane of the intestine was still adherent to the base of the pedicle. Microscopical examination showed the tumor to be largely composed of unstriated muscle and fibrous tissue, evidently arising from the muscular coats of the intestine. The cysts were due to the softening of the surrounding fibrous tissue, and were not lined with epithelium. They contained blood and clear serum.

As Dr. Condit has shown, these tumors are rare, especially so in the small intestine, but are of little clinical importance except for the possibility of their forming traction diverticula, or when provided with a long pedicle, forming a loop about the intestine and so causing obstruction.

A SURGICAL NEEDLE ENCYSTED IN THE ABDOMINAL CAVITY.

WARREN COLEMAN, M.D.

The needle which I show you this evening was taken from the abdominal cavity of a young woman who entered the City Hospital for treatment for alcoholism and chronic nephritis. She died after several weeks. Upon opening the abdomen at autopsy, the omentum was found to be adherent to the upper part of the bladder. The needle—a curved surgical needle—lay upon the omentum about one inch above the adhesion, with its concavity directed upward, and was completely encysted. It was not until the point of the needle was laid bare that its real nature was determined. The needle measured seven-eighths of an inch from eye to point. A suprapubic hysterectomy had been performed some time previously—probably a year or more, judging from the appearance of the scars—and the needle had been left in the abdominal cavity.

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DR. JAMES EWING, *President*.

PRIMARY CARCINOMA OF THE VERMIFORM APPENDIX.

D. S. D. JESSUP, M.D.

The specimen was removed at the Woman's Hospital in April, 1902, by Dr. Clement Cleveland. The patient was a woman, thirty-six years old, who had had two children and five abortions. Since the last abortion she had suffered with pain in the left inguinal region and the operation was undertaken for disease of the uterine adnexæ. Abdominal incision showed a cyst of one ovary, which was opened. The appendix was bound down with adhesions and was therefore removed. The patient made an uneventful recovery.

The gross examination shows an appendix six cm. long. At the junction of the middle and outer thirds it is bent at a right angle. There is a constriction at the bend and beyond this a dilatation giving a diameter of one cm. The proximal two-thirds are five mm. in diameter. The peritoneal coat appears smooth, although adhesions were present at the time of the operation. Section shows thickening of the wall in the proximal two-thirds, leaving a narrow lumen here. At the bend the lumen is obliterated. In the dilated portion the muscular coat appears as a thin shell and the space within is occupied by a tumor mass of firm, yellow tissue.

Microscopical Examination: Section of the tumor shows an adeno-carcinoma. The new growth has replaced the structures of the mucosa and submucosa, and its cells are infiltrating the muscular coat. The cells are grouped in alveoli of various sizes and shapes and between the alveoli is a small amount of muscular and connective tissue. In the alveoli which show a lumen, the cells are cylindrical in shape. in other places they are polygonal. The middle and proximal portions of the appendix are not invaded by the new growth, but there is a marked activity of the germ centers of the lymph nodules.

Apart from the rarity of this condition the case is of interest on account of the absence of any symptoms pointing to disease of the appendix so that its discovery was an accidental one.

A number of cases in which carcinoma of both appendix and cæcum have been found have been reported, and Kelly (1) has collected seventy-nine such cases. These, however, cannot be considered in determining the frequeucy of primary carcinoma of the appendix for there was no evidence to show that the growth originated in the appendix. Other cases of carcinoma confined to the appendix alone, I have not included in the following list because the diagnosis appears to have been made on gross examination alone. The thirteen cases collected are:

1. Reported by Beger (2). The carcinoma of the appendix was in a man forty-seven years old and was found in an operation on a sinus following drainage of an abscess in the right iliac fossa. At autopsy the abdominal lymph nodes were found to be invaded.

2. Reported by Stimson (3). The appendix, removed at operation from a woman forty-four years old, was four inches loug and in a state of "cancerous degeneration." She had had two attacks of appendicitis, the first ten years before.

3. Mossé and Daunic (4) report the case of a woman, fifty years old, who died of heart disease. The appendix, removed at autopsy, was four cm. long and four and five-tenths cm. in circumference. The new growth occupied the whole length of the organ. There was no history of appendicitis.

4. Wright's (5) case was a patient dying of general purulent peritonitis. A perforation was found at the junction of the cæcum and appendix and a carcinoma at the tip of the appendix.

5. Of two cases reported by Kelly (1) the first is without clinical history. The appendix, removed at operation, was eleven cm. long and the tumor was located in the distal portion.

6. The second case was a man, nineteen years old. An operation was performed nine days after the first symptoms of appendicitis appeared. The appendix was found surrounded by a small collection of pus. It measured five cm. in length and the tumor was situated at the base.

7. The case described by Elizabeth Hardon (6) was that of a woman, twenty-four years old. There was a

history of pain in the right iliac fossa. At operation adhesions were found enveloping the appendix. It was ten cm. long and the tumor occupied the middle portion.

8. Rolleston (7) reports an appendix removed by operation from a woman twenty-six years old, who was suffering from her fourth attack of appendicitis. The tip of the appendix was adherent to the uterus and the tumor was located here.

9. Whipham's (8) case was removed at autopsy, from a woman forty-five years old. There was no history of appendicitis and death was due to emaciation and exhaustion caused by the abdominal condition. There was a carcinoma of the base of the appendix and secondary deposits in the liver, ovary, lymph nodes, and peritoneum.

10. Of two cases reported by McBurney (9), the first was a woman twenty-three years old, operated on after a second attack of appendicitis. The appendix was four inches long and the tumor, the size of a pea, was located at the apex.

11. The second case was a man of about thirty years who gave no history of appendicitis, At autopsy, Lartigau found a carcinoma of the tip of the appendix.

12. The case operated on by Goffe (10) was a girl of fifteen years, who had had symptoms of trouble with the appendix for one year. The tumor was located at the tip.

13. Harte and Wilson (11) report a carcinoma of the middle third of the appendix. It was removed by operation from a woman twenty-four years old who gave a history of appendicitis.

The type of carcinoma in the cases where it is described is adeno-carcinoma. Nine of the cases are in women and three in men, and the fact that in most of the cases the condition is unsuspected will tend to maintain its greater frequency in women because they are more often subjected to abdominal section.

It is noteworthy that two of the cases are under twenty years of age and four under thirty years. There was a history of appendicitis in seven of the cases and no history of it in five. The location of the tumor is most often at the apex, being here in eight instances.

In four cases the new growth was found at autopsy and in the remaining cases at operation, but in no case had carcinoma of the appendix been previously diagnosed.

Routine microscopical examination of all appendices removed will doubtless in the future show that carcinoma occurs in the appendix more often than has hitherto been thought.

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8. Whitham: *Lancet.* 1901, I, p. 319.
9. McBurney: *Medical Record.* 1901, LX, p. 478.
10. Goffe. *Medical Record.* 1901, LX, p. 14.
11. Harte and Wilson: *Medical News.* 1901, LXXVIII, p, 389.

VACCINE BODIES IN VARIOLA.

JAMES EWING, M.D.

The paper is a review of the results of bacteriological examination by ordinary methods of cadavers of twenty-nine cases of variola.

Vaccine bodies were studied in the cutaneous and visceral lesions of variola by a variety of methods.

In the fresh condition the fluid from the cutaneous lesions at various stages was examined, unstained, and stained by gentian violet. By this method many leucocytes and epithelial cells and many red cells may be distinguished and set aside.

The sporocysts described by Funck (*British Med. Journal*, 1901, I, p. 448), seemed to correspond to certain large cells containing one or many greenish refractive globules. In stained smears these resolve themselves into vacuolated leucocytes and epithelia. Myriads of fine granules are usually present which stain like protoplasmic detritus.

The typical vaccine bodies are larger, spherical. homogeneous, or translucent bodies, colorless or yellowish, with or without membranes, from 1 to 7 micra in diameter. Many are extra-cellular, some within other cells. Treated with gentian violet the membranes about many of them become distinct.

By this and other staining re-agents the bodies exhibit certain polychromatic tendencies varying toward distinct basophilia. The resemblance of many of the polychromatic bodies to the red cells in the pustules which were undergoing subdivision with loss of distinct acidophile staining suggested that many of the vaccine bodies might be derivatives of red cells. The bodies with membranes and the small crescentic forms, especially, seemed to have this origin. In stained specimens some of the bodies stain blue, some red, some red on the periphery and blue in the center. These latter forms resemble the polychromasia which Maragliano described in circulating red cells.

I failed to find any traces of ameboid movements in many specimens examined on a warm stage.

In sections of the skin and mucous membranes, the main fact elicited was that the vaccine bodies are usually present in the lesions in all stages up to complete healing. They were not always present in the early necrotic foci of the tracheal and esophageal mucosa. The forms of the bodies encountered included all of those described at length by Hückel.

The bodies appeared in large numbers in the skin and mucous membranes in the petechial spots of a case of variola with ulcerative endocarditis dying in the third week of the disease. In some of these spots, however, only fragmented acidophile red cells appeared. They were unusually abundant in a case dying in the late pustular stage in which fresh hemorrhage occurred into the pustules (black smallpox). The abundance of the bodies seemed to bear a constant relation to the severity of the disease, and especially to the hemorrhagic character of the lesions. In the well-developed early pustule they were most numerous in the large flat cells on the outskirts of the necrotic zone. In the necrotic zone they were less numerous, were often found disintegrating and granular, and distinguished with difficulty. They were seldom numerous in the foci exhibiting most active degeneration. In the early stages of necrotic lesions of the trachea, many foci were found in which vaccine bodies were absent. The impression was therefore gained that if the variolous poison comes from these bodies it is distributed in a most erratic manner. Infected cells must certainly long remain alive, and in some healing lesions it seemed equally certain that many infected cells would not suffer permanently from the presence of the body. In necrosing cells the bodies were found to vary in size, to appear as rosettes, crescents, rods, and finally to break down into fragments, sometimes with vacuolation, along with the cytoplasm of the harboring cell. Sometimes the necrosing cells become condensed and present an appearance re-calling that of some sporocysts. In the necrosing epithelium of the cornea, conjunctiva, and nictating membrane of healthy dogs, I failed to find any structures resembling vaccine bodies.

The distribution of vaccine bodies was found to be co-extensive with the lesions of the disease, whether these were of the strictly variolous focal type or induced by secondary bacterial invasions. They were found in the cutaneous lesions of the pharynx, epiglotic folds, in the ulcerated nasal and ethmoidal sinuses, very abundantly in the trachea and bronchi, in the esophagus, in circumscribed or diffuse ulcerations of the stomach, abundantly in the intestine, and in the renal pelvic epithelium.

I examined various lesions of the skin and mucous membranes to determine if vaccine bodies are present in other than variolous processes, and while never finding in any other lesions great abundance of bodies resembling the vaccine corpuscles, I found a scanty or moderate number of structures indistinguishable from vaccine bodies in streptococcus inflammation of the skin, in erysipelas, in pemphigus, in dermatitis herpetiform, in purpura hemorrhagica, and in measles,

In the decaying skin of variola, the vaccine bodies disappeared without sign of multiplication between the fourth and eighth days.

THE ORIGIN OF VACCINE BODIES.

Some vaccine bodies seem to give evidence of an origin from the cytoplasm of the epithelial cells. This is especially true of those bodies which are connected with the cytoplasm of the cell by radiating fibres, and of those forms which exhibit a central basophile mass fringed by a peripheral acidophile portion. Yet the smallest and presumably the earliest vaccine bodies do not exhibit these radiating threads, but are extremely well-defined from the cytoplasm and impress the observer as being distinctly foreign to the cell. Hückel had some difficulty in adjusting his theory of a cytoplasmic origin to the appearance of these small compact bodies.

My belief that many of the typical vaccine bodies in human tissues are remnants of red cells has been reached very slowly. It first appeared in the study of human material that vaccine bodies were most numerous in the hemorrhagic lesions, and that by some stains—*e.g.* Heidenhain's iron-hematoxylon—the vaccine bodies behave very much like red cells. Distinct transitional stages between red cells and fragments and basic vaccine bodies were not encountered until late in the series, when a trachea which had been hardened in Orth's fluid (Müller-Formalin), exhibited a great variety of forms which resembled red cells in their tendency to stain with eosin more than the usual vaccine body.

Likewise, in a late secondary hemorrhagic case, in which recent profuse hemorrhage had occurred into the pustules, a great variety of forms, apparently transitional between red cells and vaccine bodies, were found in and between epithelial cells.

Finally, in the renal pelvic epithelium of two primary hemorrhagic cases was encountered a profuse display of the englobement of red cells and their fragments by epithelia, and their transformation into polychromatic vaccine bodies. Here were found red cells unaltered, within and between epithelial cells—large red cells with beginning or advanced vacuolation, some strongly acidophile, some strongly basophile; all sizes of acidophile fragments; some epithelial cells holding within the same vacuole various shades of acidophile and basophile fragments of red cells, englobed red cells with basophile centers and acidophile peripheries, or fragments fringed with protoplasmic or hematoidin granules. These polychromatic qualities were best demonstrated by staining with strong hematein and strong watery eosin, With dilute eosin most of the bodics remained tinged with hematein. By methylene blue or Nocht's method, the bodies usually stained light or dark blue. Their perinuclear position and distinct halo were identical with those of the typical vaccine body of the cornea.

The above observations, which were readily dupliated by a review of the previous material, seem to place beyond donbt the conclusion that red cells may be, and very frequently are transformed into bodies indistinguishable from vaccine bodies.

Yet in specimens fixed by Müller's or Orth's fluid, strong staining in watery eosin develops a certain acidophile tendency in many of them although leaving the nuclei of epithelia and leucocytes uniformly dark blue.

The belief that many vaccine bodies are derived from red cells accords with many facts concerning the occurrence of these bodies and the changes which may affect red cells. Two familiar types of degeneration of red cells occur in the circulating blood in various conditions, especially in cases of severe streptococcus infection. They are first, polychromasia of Maragliano, in which a central basophile portion of the red cell separates from a broad peripheral portion containing all of the hemoglobin remaining in the cell; and second, polychromasia of Gabritschewsky, in which the entire cell stains a brownish color after treatment with eosin and methylene blue or eosin and hematoxylon. Punctate basophilia and schistocytosis or subdivision of red cells with the appearance of basic centers of the fragments also frequently occur in the circulating blood. A pronounced case of this latter type has been described by K. Ehlich and Lindenthal (*Zeit. f. klin. Med.*, Bd. 30, p. 427), in nitrobenzol poisoning. The basophile portion is regarded as the remnant of nuclear material in the red cell. Now, all of the above changes in the red cells occur in very unusual abundance in and about the focal lesions of variola and vaccinia. In the earlier stages of the lesions the necrosing tissues and their vicinity are literally drenched with fragments of subdivided red cells exhibiting various polychromatic staining qualities. I have seen no other type of lesion in which such active destruction of red cells occurs about necrotic foci.

Hence, about the inflamed cells of the various lesion of epithelium there are a great abundance of already altered fragments of red cells, which, when englobed by the epithelia at once possess the characters of vaccine bodies.

The somewhat specific quality of this destruction of red cells about the variolous lesion may explain the abundance of vaccine bodies in such foci, which is practically a pathognomic feature of variola,

The perfectly homogeneous quality of the majority of vaccine bodies has suggested that they represent a form of hyaline degeneration of the cytoplasm; but the sudden appearance of these compact masses in the cytoplasm of epithelia has distinctly impressed the minds of most observers, including Hückel, with the idea that they must be bodies foreign to the cell. The granular edges of some of the bodies may be referred to the disintegration of the outer rim of the red cell, while the pseudo pods of vaccine bodies are identical in appearance with the knobs on shrinking and deformed poikilocytes. Sometimes there is a rim about the compact vaccine body such as exists also about hardened and densely stained fragments of red cells. The occurrence of hematoidin granules about the halos of some vaccine bodies is an unusual but unmistakable suggestion of the true origin of these particular individuals.

While it seems certain that many bodies now passing as probable parasites are remnants of red cells, before attempting to extend this theory of origin to all vaccine bodies it is clearly necessary to demonstrate such a relation for the vaccine bodies in the corneal epithelium. Here, in a bloodless tissue, it seems hardly possible that red cell detritus can account for the great numbers and comparatively wide distribution of vaccine corpuscles. Hence, the theory of the existence of a specific form of vaccine body, possibly parasitic, remains almost untouched.

That the vaccine bodies of the cornea are not derived from red cells forced into the epithelium from the lymph spaces communicating with the canal of Schlemm, is practically certain, because these lymph spaces in corneal vaccinia, at least in the centers of the cornea, are usually free from red cells. Another possible mode of origin is from the abundant red cell detritus of vaccine which might account for the bodies seen in one inoculation wound, but Wasielewski claims to have transferred vaccine from cornea to cornea through forty rabbits, finding the vaccine bodies undiminished in each case. These results, if correct, indicate that the corneal vaccine body is either a parasite, or, as Hückel believes, a derivative of the epithelial cell.

Considering the very peculiar conditions of nutrition of the corneal epithelium pointed out by Ranvier, it may very well be that entirely different processes take place in these cells and in vascular human tissues, and that the vaccine bodies of the cornea are entirely different from those of other tissues. Against this possibility is the very great similarity between all typical vaccine bodies, while the results of the present study still further complicate the subject by indicating that red cell detritus may assume forms apparently indistinguishable in position, morphology, and staining re-actions, from typical vaccine bodies.

Possibly some method may be secured by which one can distinguish red cell detritus from vaccine bodies; or, on the other hand, some facts may be gathered pointing to the possible access of red cell detritus to the corneal ulcer.

STUDIES ON THE ETIOLOGY OF VACCINIA AND VARIOLA.

ANNA W. WILLIAMS, M.D.

The studies reported in this paper may be divided, according to the methods employed, into two parts, first bacteriological and second histological.

The direct object of the bacteriological studies has been to determine if an organism in pure cultures could be obtained which would produce typical vaccinia or variola, while that of the histological studies has been to determine the nature of the "vaccine bodies."

In the bacteriological studies the plan of work was as follows:

1st—Studies of serial and isolated smears and hanging drops from eruptions on rabbits, calf, monkey and man, from corneas of rabbits, from fresh and old glycerinated vaccine virus and from filtered lymph.

1nd—Cultures made from all of these materials but especially from the inoculated corneas of rabbits and old glycerinated vaccine virus, using ordinary and special media. The ordinary media were used as controls. The special media used were, (1) ascitic-broth, ascitic-broth in celloidin capsules inserted into the peritoneal cavity of the rabbit, (2) wounded peritoneum and subcutaneous tissue of vaccinated and non-vaccinated rabbits, (3) rabbits skin in the peritoneal cavity of the rabbit, (4) foetal rabbits skin taken with aseptic precautions, (5) fertilized hens' eggs.

The most interesting results were obtained from the inoculated rabbit corneas. These experiments are still in progress. The technic is as follows:

The corneas are inoculated with old glycerinated virus and, after a varying time, the animals are killed, the eyes removed under aseptic precautions and washed in sterile broth. The whole cornea is then cut out, washed in successive sterile broths, placed on an agar plate and kept at 36° C. over night. If there is no apparent growth the next day, the cornea is placed in ascitic-broth after smears and hanging drops have been made from the inoculated area, and returned to the thermostat. After 24 hours much of the epithelium has become loosened and on shaking the ascitic-broth becomes slightly cloudy with apparent irregularly granular detritus. Microscopically, besides much finely granular material there are seen a few vaccine-like bodies free and many epithelial cells and leucocytes in various stages of degeneration, some of the former still containing vaccine bodies.

The ascitic broth containing these cells, vaccine bodies and granules when rubbed on freshly shaved rabbit's skin produces a typical eruption.

The chief points of interest in this cultural study of the corneas are, first, that it has given us a method for obtaining active vaccine virus unmixed with discoverable organisms, and second, that it shows us the vaccinia is not produced by an organism or a combination of organisms growing rapidly in ascitic-broth.

The histological studies were made principally upon rabbits corneas. The sections were prepared by Dr. Flournoy.

Control inocculations were made with (1) inactive vaccine virus, (2) filtered vaccine virus, (3) a very large coccus isolated from vaccine lymph and having forms similar to many of the vaccine bodies and (4) the tiny bacillus and (5) the large cocco-bacillus spoken of in the first part of the paper.

From the study of the corneal sections it was shown that:

1. The epithelial cells of the cornea may be phagocytic for leucocytes, red blood cells certain bacteria and variously sized and shaped, chromatin-staining bodies, the so-called vaccine bodies.

2. Apart from the above inclusions certain degenerative changes may appear in the epithelial cells.

3. All of these appearances are most frequently seen in the perinuclear zone.

4. The "vaccine bodies" appear regularly after inoculations of active vaccine or variolous lymph; they do not appear after inoculations of any other substance tried.

The principal observations from these studies may be summarized as follows:—

1. The specific virus of vaccinia grows readily in

the corneas and the skin of rabbits, producing in the latter situation the typical eruption.

2. Ascitic-broth containing the epithelial cells from corneas which have been inoculated with old active vaccine lymph produces the typical eruption of vaccinia, though no organisms can be demonstrated in the ascitic-broth mixture.

3. Such corneas show as the only constant, characteristic appearance, and so-called "vaccine bodies."

4. Vaccinia is not due to any organism or combination of organisms growing readily in ascitic-broth.

Discussion.

DR. EWING: The contribution just read shows evidence of such a volume of work conducted on such a judicious plan that I feel that Dr. Williams and her colleagues are to be congratulated upon it. It was a specially important result that Dr. Williams was able apparently to demonstrate an increase of the virus in ascitic broth to which infected corneas had been transferred. Regarding the isolation of various bacteria from vaccine and variola, it is to be noted that we are in the habit of casting aside as unimportant cultures which are occasionally encountered. It may well be that some of these demand further attention, and although previous work in this field has been extensive, it still remains important to thoroughly test as many of these species as possible. The great difficulty of determining the presence or absence of specific effects from such bacteria has led to many erroneous claims for bacteria occasionally occurring in vaccine and variolous exudates; *e. g.* Martin's, Nakanishis', etc.

I had some experience with these difficulties with a bacillus, which I called Bacillus 19. It resembled in morphology and in the fluidification of blood serum, that described by Martin in 1893. Dr. Park kindly loaned me a calf with which to test this bacillus. Vaccination with Bacillus 19 was negative, and a culture was injected subcutaneously, producing an abscess from which after two weeks the germ was recovered pure. The first attempt to vaccinate this calf with active vaccine failed, but a subsequent vaccination made very thoroughly produced a "dry take." From this "dry take" a second calf was vaccinated also with an unsatisfactory "dry take." Both of these calves were vaccinated the second time and each gave as good a take as after the first vaccination. These results on the calves being unsatisfactory, the bacillus was finally set aside when it was proven inert on monkeys.

I was also interested in Dr. Williams' observations which favored the belief that red cells might become transformed into vaccine bodies.

PRELIMINARY REPORT OF EXPERIMENTS WITH FILTERED VACCINE.

WM. H. PARK, M.D.

As is well known, attempts to produce vaccination with the fluid which had passed through a Chamberland or Berkefeld filter have uniformly failed. The present experiments were undertaken with the idea of using crushed virus and of concentrating the filtrate. It was thought to be conceivable that the vaccine organisms might be small enough to pass through the filter and still, because of being contained in the epithelial cells, they might not pass, the cells themselves being held back.

It was also thought possible that the filtrate might contain a few vaccine organisms, and yet have an insufficient number to cause a vaccination. If this condition existed, it seemed possible that by quickly evaporating the filtrate, sufficient concentration of virus might take place to produce vaccination. The following experiments were tried:—

Fresh virus was dried over sulphuric acid in a vacuum. This vaccine material was crushed up with fine sand, using a pressure of twenty-five tons to the square inch. This material was rubbed up with water and separated into two portions. One was drawn through a Chamberland, the other through a Berkefeld filter. Both filtrates were evaporated over sulphuric acid in a vacuum. Calves and rabbits inoculated failed to take. Similar virus was crushed with the sand twice and again six times. The filtrate from this material failed to take. Ordinary glycerinated vaccine and active serum from calves were filtered and failed to take in calves or rabbits. All these calves were kept in a special building belonging to the Department of Health where no possible contamination could occur.

The calves treated in the same way in the vaccine building developed a few typical vesicles, but these are believed to have been due to contamination from the other calves and not to substances which passed through the filter.

THE RELATION OF STREPTOCOCCUS PYOGENES TO VARIOLA.

JAMES EWING, M.D.

From the routine bacteriological examination by ordinary methods of the cadavers of twenty-nine cases of small-pox, the streptococcus pyogenes was demonstrated in the heart's blood in all cases, and in the cutaneous lesion of about ninety per cent of the cases. This result with the heart's blood is only in accord with the results of some previous studies, as Le Dantec (*Arch. de Med. Navale* T. 64, p. 410) obtained the streptococcus in the heart's blood of fifty consecutive cases.

The abundance of the growth was uniformly proportional to the severity of the disease, and in the primary hemorrhagic cases the cultures were remarkably profuse.

In two cases the streptococcus was associated with the Klebs-Loeffler bacillus, in subjects exhibiting extensive tracheal diphtheria; and in two cases dying late in the disease, with much ulceration of the skin, staphylococcus aureus also grew. Once a special bacillus, called Bacillus 19, was also obtained. In five cases, cultures of ten c.c. of circulating blood were examined with a negative result. Only one of these cases was fatal.

Arnaud, however, reports finding the streptococcus in the circulating blood in two primary hemorrhagic cases (*Rev. de Med.* 1900, p. 303). The demonstration of the streptococcus in the cutaneous lesions in nearly ninety per cent. of these cases indicates the very general presence of this organism in these lesions. Perhaps more careful technique would have given more uniform results, as chain cocci were twice found in sections of the skin when cultures were sferile.

Most of the autopsies were performed within one to six hours after death, and while there was opportunity for post-mortem development in some cases examined after a longer interval in hot weather, the usual abundance of the streptococcus did not fail in early autopsies in very cold weather.

The uniform presence and especially the remarkable abundance of the streptococcus in the cases seems parallelled in no other conditions except in scarlatina and puerperal septicaemia, while the histological lesions indicate widespread effects of the growth of this micro-organism similar to those of pure streptococcus infection. This is especially true in the primary hemorrhagic cases in which the bacteriological and histological study of the cadaver strongly indicates that the streptococcus overshadows any other micro-organism that may be present.

These conditions have led me to conclude that it will always remain impossible to reproduce the fulminant type of variola without the aid of this micro-organism.

When the streptococcus is present in the circulating blood in enormous numbers and on the second or third day of a disease, the question naturally arises whether the presence of this micro-organism in the disease should be classed as a simple secondary infection. Nevertheless, the known facts do not warrant the assumption of a necessary symbiosis because vaccine produces specific lesions when no streptococci can be demonstrated in the virus. The condition seems very nearly like those described by Schleich as "syntoxic parasitism," although present indications favor the belief in a micro-organism too small to be seen with the microscope rather than in the purely chemical nature of the specific virus of small-pox.

A further review of clinical features of small-pox demonstrates other interesting relations of the streptococcus to the disease. In two cases, general scarlatiniform eruptions developed during the course of ordinary discreet variola. One of the cases died in the children's ward in which no further cases of this sort developed. The other went through the usual course of scarlatina with profuse scaling desquamation, but later developed multiple abscesses in the skin. These cases were, therefore, probably not true scarlatina, but examples of the scarlatiniform septic eruption due to the streptococcus which was abundantly present in both.

Three cases of ulcerative endocarditis were encountered with the usual abundance of streptococci in the heart's blood. One of these gave cardiac symptoms from the first and died on the eighth day with extensive ulceration of the mitral valve and a rather scanty eruption.

Finally, erysipelas and diffuse phlegmonous inflammation of the skin are very common incidents in small-pox hospitals.

In these various clinical features of the disease the streptococcus exhibits its well-known capacity to produce a great variety of specific clinical effects, and in them it seems to follow the ordinary rules governing secondary infection. In these clinical forms of the disease it is interesting to note how this micro-organism can multiply in the system; first, as a complicating factor in the cutaneous lesion of small-pox; then as the excitant of a scarlatiniform eruption, then, under the form of pyemic abscesses, or as ulcerative endocarditis or erypsipelas, etc., while none of these manifestations seem to confer any immunity to the subsequent attack of the micro-organism in another clinical from.

Discussion.

Dr. Park: Dr. Ewing has demonstrated that in a large series of fatal cases streptococci were universally present in the blood and in the pustules of the skin aud mucous membranes. It seems to me he goes too far, however, in thinking that the streptococcus is necessarily present before the symtoms and lesions which we find in small-pox can develop. Both scarlet fever and small-pox cause marked changes in the mucous membranes of the throat. Here we have the streptococci regularly present. The profound changes produced by the poison of variola combined with the location of the streptococci seem to me to account for the secondary infection of the streptococcus. If no streptococci existed, I believe we would still have severe and probably fatal cases of small-pox.

Dr. Ewing: My own ideas regarding the relation of the streptococcus to variola are by no means clear, but I have been greatly impressed with very early appearance and enormous development of the streptococcus in the disaase. Its behavior in the primary hemorrhagic cases and in some other forms seems different from that of an ordinary secondary infection. I do not find either that the term "symbiosis" is justified by the facts. It would seem that the small-pox virus annihilates resistance to the growth of the streptococcus, with results which occasionally resemble fulminant puerperal septicæmia, where the streptococcus is the only micro-organism present. Perhaps Schleich's term "syntoxic parasitism," most closely expresses what seems to me to be the condition in primary hemorrhagic small-pox.

As to the relation of red cells to vaccine bodies, I am not prepared to claim that all vaccine bodies are derivatives of these cells, but having found that in the tissues the fragments of red cells are a very common origin of vaccine bodies, I am inclined to think that all vaccine bodies may have the same origin. In the cornea it seems almost hopeless to attempt to prove this origin, in which case the theory of the exclusive origin of vaccine bodies from red cells must fail of demonstration. I have already found that red cells are present in the inoculation wounds of the cornea under somewhat surprising conditions. Therefore, considering all the evidence against the parasitic nature of vaccine bodies, at a time when some Continental observers are grouping carcinoma and variola together, it seems justified to urge that some and possibly all of the appearances on which this relation is based are referable to red cell detritus.

THE CHEMICAL THEORY OF SMALL-POX.

W. S. MC GILL, M.D.

To rehearse before the members of this Society the history of our present etiology of variola would be for the most part but wearisome repetion if reviewed in full. With your permission then, I will allow myself to pass rapidly over the multiplicity of details.

Let us recall that, in small-pox we have one of the most ancient of the eruptive plagues, the longest known of contagious diseases, and the pioneer in our conception of immunity as a possibility long before its rational basis and fundamental components were even thought of.

More than two centuries ago it was a well credited fact that small-pox was an infectious disease, The strict limits of its contagion have been drawn more closely and more insistently urged with each advancing step of epidemiology; but only gained their firm establishment with the advancement of our knowledge of bacteriology.

In the first glow of germ discovery, the bacterial origin of all infectious diseases was widely proclaimed and still more generally credited. The numerous announcements of the specific coccus, bacillus or other bacterial origin of variola have not yet reached the end of the list, nor the final withdrawal of their rival claims; but their very numbers have succeeded in creating a widespread scepticism as to their scientific value and a strong insistence that no further immature investigations be brought out.

With a full realization of the benefit of working in times of such prevalling scepticism, it is particularly advantageous to examine very carefully the grounds on which a claim for the bacterial cause of small-pox can rationally be placed.

Remember the length of time during which this disease has been particularly distinguished as due to a *specific virus*, its possibilities of attenuation, inoculation, vaccination and resultant and acquired immunities, communicability from human to animal races and reciprocal attenuating action.

With the exception of the determination of a specific organism, its culture in vitro, and subsequent inoculation to reproduce the clinical form of this specific disease, we have had for years, in variola, a typical picture of a bacterial infection of the human being. With the exception of the results of the work of Bosq and Roger, to be considered in a moment, bacteriology has, by the failure to identify the specific germ in strict accord with its well-known rules for such scientific investigation, no claim to include in its family the determining agent of variola.

The close resemblance of the symptomatology of variola to that of typical bacterial infection of man, makes it easy to understand that the first move of the incipient promulgator of a theory of such infection would turn to variola; to find there most easily the requisite bacteriological proofs. What has been the result of his inquiry? Thirty years of close investigation, in some cases, by the best bacteriologists of the world, have totally failed to demonstrate any form of bacterism entitled to the slightest claim of specificity.

Nevertheless, the facts are fully demonstrated (without denying the possibility and frequence of a secondary bacteriological infection of the variolic pus) that variolic fluid is often found, containing no bacteria discoverable by any known method of stain or culture. Such fluid, often pus, will nevertheless invariably reproduce the specific disease when inoculated to the proper receptive medium. These positive inoculations of material absolutely deprived of bacteria have been made: in case of a hemorrhagic variola, the blood drawn from the vein at the elbow, one hour before death; again, with material from certain visceral lesions,·in which the total absence of bacteria was assured by multiplicity of tests of stain and culture; and also by inoculation of similarly verified, bacteria free, sero-purulent liquid, obtained from the vaginal tunic during the course of variolic orchitis.

It has been amply demonstrated elsewhere that such pus and the blood of hemorrhagic cases inoculated into animals may be continued in series, inducing a subsequent immunity to variolic inoculation and in some, provoking death.

Blood from a case of hemorrhagic variola has for a long time been carried in a continuous series of animal inoculation and re-inoculation, at the Carnegie Laboratory, and invariably provokes a fatal disease, in our chosen animals, and of a determined type with persistence of characteristic lesion. What we are gathering are the data to prove it to be the specific agent of small-pox.

To prove the bacteriological origin of variola, it is but natural to attempt to introduce another cause. The protozoon is thus advanced; first by Renaut, in 1881, followed most prominently by Van der Loeff and Pfeiffer.

The first to make the subject of a protozoic etiology the question of direct experiment seems to have been Guarnieri.

Numerous workers since that time have very well established that in the various organic liquids of a variolic subject and in vaccine, also in certain of the tissue cells, noticeably the epithelial, and producible there by the inoculation of variolic pus or vaccine are small, characteristic elements, the so-called variolic bodies. To properly interpret the nature and significance of their existence constitutes a very important point of discussion in any consideration of variola at the present time.

The conclusion of the question whether these minute corpuscles are parasites or simply derivatives of tissue cells does not appear to be furthered by the confinement of experiment to the inoculation of corneal epithelium. For several investigators, myself included, report the irregularity of corneal reaction even to known virulence of the inoculated material. Moreover, the bodies there found and frequently offered as typical so-called variolic bodies, have been produced by experiments of purely traumatic nature. The exhaustive study, by Ranvier, of the special tendencies of the epithelial cells of the cornea to heal a traumatism in such peculiar manner as to make inevitable an accumulation of both extra- and intra-cellular minute staining bodies, known to be of nuclear debris origin, would seem to make it imperative upon the conscientious experimenter to choose some other epithelium than this for decisive investigations of a question absolutely depending upon the elimination of a possibility of cell-debris being mistaken for parasites. Without entering upon the question of debris *vs.* parasite as it should be considered, it can, I think be fairly stated that many demonstrations of the so-called bodies in the cornea were probably only cell-debris. It is my own personal opinion that such is the real origin of all of the corneal bodies, that it has been my opportunity to examine. In defense of my opinion may I be permitted to add that experiments to invalidate the proposition of cellular residues should not be executed in that particular point of epithelium (the corneal) which Ranvier has so explicilty shown, inevitably heals its wound by a process, peculiar to that tissue and of necessity depositing at the locality of the traumatism, a mass of disrupted cell components, even nuclear fragments.

Returning from the digression, let us resume that, the question at issue is in substance: first, are these minute corpuscles parasites or derivatives simply of re-existing tissue cells or to further elaborate, are they nuclear debris resulting from the death or possibly chemical disruption of the cells, or as Dr. Van Gieson puts it in tentative suggestion; are these degenerative or atavistic cellular elements resultant from the changed chemical or physiological action of the surroundings, or produced by the invasion of a parasite, or are they the adventitious or specific organisms themselves?

The line of investigation to determine this question has been long varied and thorough. Some of it admirably true to the scientific method of research, but possibly through slight lack of system, perhaps not receiving the notice it deserved, seems to have failed to attain the goal as rapidly as it promised.

Some of the reports of the small-pox investigations have come out recently at Washington, some you have heard this evening. But even to mention the names and subjects of the workers of the last few years, is beyond the limits of this paper.

Standing out in strong relief from all other recent investigations, are those of Bosq and Roger in France. Here with the most explicit statement of laboratory experiment, are to be found all of the steps of identification of a specific organism. Here is research work in strict conformity with the limits of identification prescribed by Microbiologists. We can but say that the reports of Bosq and Roger seem to have contributed the most important data for the adherents of the protozoic element as the specific microbe of variola.

The variolic bodies are to be found in the blood of hemorrhagic cases before their eruption, and the blood containing them is proven to cause the variolic infection, when drawn from the patient as early as the third and fourth day of the incubation period of the disease. From the first and second day of eruption, up to the stage of suppuration, as the degree of the power of contagion increases in geometrical ratio, the specific elements appear and increase in the hematopoietic organs; and then, in the epithelial membranes (skin und mucosa), papules becoming vesicles and subsequently pustules are found, without the occurrence of the slightest contamination of adventitious bacteria detectable by any stain or culture.

The desquamations, excreta (including the urine in cases of hematuria), all organic fluids and residues reached by the blood of a variolic patient contain the special bodies.

They are exceedingly resistant, and if really the specific element, are proven by direct experiment to survive air-desiccation for at at least two years. They retain an unimpaired power of contagion, after exposure to the intense cold of evaporating liquid air, after subjugation to the hydraulic pressure of 4000 pounds to the square inch, and even after heating for a limited time to the vicinity of 70 degrees C. The resistance of the germs of variolic contagion to the fumes of sulphur, as usually employed in the disinfection of mail-matter is insisted upon by Roger, and by him it is shown that this survival of the contagion is inevitable, unless the fumes are brought into the most direct and prolonged contact with the sulphur vapor.

The transmission of the specific microbe to the fœtus has twice been demonstrated by actual examination of organs involved. In two cases of abortion, one at the fifth, the other at the sixth month of pregnancy (the mothers suffering with confluent small-pox), the amniotic fluid and the fœtal tissues themselves revealed the presence of the described specific microbe of variola. In fact this connection it may be well to draw attention to the that infection of the fœtus is rarely noted as apparent previous to a delivery during the ninth month of the intra-uterine life. With the increased knowledge, to be derived trom the experimental study and verification of its specific agent, it is recognized that the period of incubation is in animals a somewhat variable quantity and the same is true at the beginning stages of human life. The birth of a child, whose first eruption follows at least 30 days later the first appearance of the maternal infection, is a fact well established. Moreover, it is striking to notice that the pronounced type of acute and anemiating septicemia with variola presents in many of our experiments with animals, accentuates this side of its action as the resistance of the organized animal form is rendered lower in our line of experiments: this septicemic type of variola is strikingly predominant in the fœtus and very young child. The form of variolic infection without the slightest eruption is well known to all students of this disease in the rabbit. The comparatively frequent occurrence of a like infection is one of the common notes of the clinic relative to new born infants. The possibility of this origin of the so-called natural immunity is here suggested.

In the usual course of infection, the specific organisms penetrate the respiratory tract, where if successful in traversing the bronchial epithelium, it enters the blood, by it is diffused throughout the organism, in it lives and multiplies, producing the well known symptoms of variola; a veritable general toxemia, of which the eruption is the mere epithelial reaction or method of excretion, as subsequent investigations may determine.

The juices of the digestive tract destroy the parasite. They are likewise incapable of penetrating the intact cutaneous epithelium, but invade rapidly the slightest denudation of that surface.

According to the numbers of the originally infecting organisms, the depth of the cellular lesions produced is variable. The blood is always profoundly altered, marked by a characteristic mononucleosis, the discovery of which is considered sufficient evidence on which to base a doubtful diagnosis.

To prevent the danger of extending this paper beyond its time allowance, it is necessary to turn aside in order to present to you, an outline of chemical study of the question.

In order to more exactly outline the determinant factors of the variolic symptomatology, as well as the bearing of such factors on the etiology, I have devoted a considerable amount of time and effort upon purely chemical considerations of variola.

The results of that work have surpassed my expectations in some respects. They have also brought me face to face with many difficulties to such an extent that it is now only possible to mention some of the lines and the partial development so far attained.

The chemical study was most strictly confined to the vaccine matter furnished by Dr. Park, from the Research Laboratory of the Health Department of the City of New York.

The samples were of pure vaccine pulp, as scraped from the calves, and also from the prepared (glycinerated) pulp. Every sample was carefully analyzed for matter of alkaloidal nature and in two cases were positive in results.

By processes of multiple solvents and separations, in both of these cases, it is found that we have to deal with an hitherto unidentified alkaloidal substance. Portions of the most purified material to be obtained are to undergo ultimate organic analysis as soon as possible. From every sample of vaccine matter were obtained diastasic material, but of great variability of composition and properties. Among them are apparently three distinct types of diastase. There is one which slowly but directly acts upon the protein matter, one which is very stupefying to the experimental animal when injected intravenously, but does not seem to retain any permanent effect. In this connection, I must add however that no observation of the phenomena of nutrition were made in these experiments; and these would seem to be very imperative, with a view to determining the extent of chemical influences in provoking the anemic and wasting phenomena of the sub-acute type of disease which variola itself reveals in the animal.

The third type of diastase isolated from the vaccine samples was most peculiar. Injected intravenously into rabbit and guinea-pig, it provoked a very rapid and startlingly violent convulsion. A prelude of fibrillary tremor, collapse to one side resulting in the fall of the animal; this was followed by periodic muscular twitchings of less and less violence, a final repose and ultimate recovery in from thirty to forty minutes. Further experimentation of this diastase was impossible by reason of the limited supply of the material. And constant attempts to find it in another sample have thus far failed.

As you will easily realize the short time at our command thus far in work of such nature has permitted the collection of a number of these peculiar chemical substances; but has given us, as yet, very little time for the study of their nature. We must go very slowly, for it is untrodden ground, and our material is very limited in quantity and hard to obtain. It seems to be an exceedingly difficult problem to find any two of these substances which are exactly alike.

In order that the bearing of such investigations be understood will you permit me to call your attention to the increasing realization of the predominant role of the chemical problems in majority of our infectious diseases. The questions of immunity, serumtherapy, and scientific vaccinations depend upon them. It is a tenable position to take that the tissue lesions, the cellular and nuclear debris, the degeneration and atavistic retirement of cells, about which so much is said, are most directly resultant to the purely chemical influences of the affected tissue's surroundings.

To determine the proper sphere of influence of the chemical forces in question is the scope of our chemical investigation of the variola problem. Its difficulties can be no proper deterrent, for the importance of its determination is pre-eminent. There lie the secrets of the true pathology of so septicaemic a disease as this; and there, too, are to be found the facts which will permit the realization of rapid and real immunity.

Regretting that I have not the time, and perhaps this is not the place, for presentation of such chemical investigations in detail, it remains to close with the statement of conclusion that the ferment substances of vaccine matter are extremely alterable, limited in activity and amount when compared to the like substances of the variolic tissues. Consequently, the more promising field for such chemical studies is to be found in freshly infected variolic tissues. These are now being used and already show less variability.

DEMONSTRATIONS OF THE SKIN LESIONS OF SMALL-POX.

S. POLLITZER, M.D.

A remarkable and most instructive series of lantern slides of the gross and microscopical lesions of variola were demonstrated by Dr. Pollitzer.

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DR. JAMES EWING, *President*.

OBSERVATIONS ON MALARIAL PARASITES.

L. B. GOLDHORN, M.D.

In protracted cases of tertian fever, certain forms of the parasite are quite constantly met with, which differ essentially from the ordinary ones of the asexual cycle. They take no part in segmentation, and they are never seen in the recent primary infections. At least two of them are the analogue of the crescentic and ovoid bodies of tropical malaria; they are the macrogamete and the microgametocyte of tertian fever. They are readily recognized when fully developed, in the following manner: in smears treated with chromatin dyes, the male or microgametocyte is a rather large parasite with large achromatic zone, in which a mass of unevenly staining chromatin lies in the form of filaments. The parasite's body takes the basic dyes poorly and its coarse, blackish pigment is brought out more distinctly than in any other form. It never has multiple chromatin bodies. In the moist chamber it flagellates and the flagella originate within a limited area which corresponds to the zona achromatica. Before it flagellates, its usually quiescent pigment beomes unusually agitated. It disengages itself from the corpuscular remnant, assumes a spherical form, and flagellates. In stained preparations many variations in the position of the chromatin mass are seen, but on the whole the characteristics remain those given. The female or macrogamete is still larger when fully developed; in the chromatin stained smear it presents a large well stained body with or without corpuscular remnant and a small irregular chromatin mass in a poorly defined zone situated rather constantly peripherally, rarely ever centrally, but at times just within the body. Its pigment is somewhat finer than that of the microgametocyte. A third form has a round chromatin kernel well within the parasite's body. This kernel is surrounded by a lightly stained reticulated area which also takes on the chromatin dye and is therefore pink. The body of this form stains well with methylene blue and it is usually smaller than the two forms just described. I have never seen it extra corpuscularly, and believe it to represent no phase of the schizogony, as I have never met with it in recent primary cases. Much confusion arises from the promiscuous study of parasites in cases of relapse, or old cases. Many typical forms are seen, such as multiple chromatin bodies in young forms, premature segmentation, abnormal position of chromatin, and queer positions of the parasites on the corpuscle. But the number of segments (schizonts) varies even in perfectly fresh cases. As each young parasite receives an equal share of the mother's body and as there is no waste apart from the transformed haemoglobin and corpuscular remnant, it seems to me that the number of segments depends upon the size of the infected corpuscle and upon the amount of nourishment it contains. (Double infections of one corpuscle might also be considered, but frequently one parasite atrophies). As the parasite forming the greatest number of segments might require more time for the completion of the cycle than one forming a small number only, it would by segmenting later fall behind the other parasites. This irregularity, if exaggerated, might influence the length and periodicity of the paroxysms. As a matter of fact one can find segmenting bodies for some time after a chill, and sometimes the duration of the chill is protracted in advanced cases. By diligent study of animal malarial parasites I have found much which has led to a better understanding of human malaria. In a paper read before the University Medical Society I described a parasite found in a species of African monkey. I have since had occasion to study the parasite again and now feel certain that nearly all forms seen by me were gametocytes. What I stated about the staining and chromatin characteristics of the human tertian parasite is, in the monkey, still more clearly defined; and the third form with karyosome and paler staining reticulated area is readily found. Febrigenous forms were not seen. Bone marrow and spleen contained no segmenting bodies. A peculiar notch at the edge of this last (third) form and of the macrogamete was rather constantly observed and helped to confirm the belief that these third forms are related to the gametes, and most closely to the macrogametes. The parasite obtained from the monkey is probably the analogue of tertian fever. In birds with Halteridium infection one sees the above enumerated characteristics of gametocytes. The staining differences and those in the chromatin are pronounced. The microgametocyte stains very poorly, has a very large central achromatic zone and more or less polar pigment; in the achromatic zone lie delicate filaments of chromatin. The deeply staining macrogamete has, on the other hand, a small chromatin mass usually at the edge in a small achromatic zone, and the relatively finer pigment lies all over the body of the protozoon. I believe these "hantelforms" to be the analogue of the human estivo-autumnal gametocytes, the so-called crescents. Several preparations in my possession show some details in crescentic bodies which I have not seen demonstrated before. If the pigment be removed from these gametocytes a large achromatic zone becomes wonderfully distinct; in it lies the chromatin always in a single body, never split up into segments. As a matter of fact, I have never seen evidence of parthogenesis in crescents. There are some curious differences in the staining of crescents; some have marked polar staining, others stain lighter blue throughout. It is possible that the one staining deeper may be the female. This year it was impossible to obtain cases with crescentic bodies and experimental work that had been planned had to be abandoned. Most instructive material was, however, obtained in the form of tertian cases. Only a brief review of the more interesting cases may be given. An old case of one and a half year's standing with frequent relapses showed only a few queer young forms and many gametocytes; no parasites with multiple chromatin bodies were found. Another case of seven weeks' standing with rich infection showed an unsual number of corpuscles with two parasites maturing side by side, or one developing at the expense of the other. A case of a woman from Coste Rica, where the malaria was contracted, was most instructive because no strictly normal segmenting bodies such as one is accustomed to find in the recent primary infection were seen; instead there were ring forms with small accessory chromatin body in the thickened portion of the body, or two, three or even five unevenly staining, large round chromatin bodies in a large ring of even diameter throughout. There were never more than twelve segments, usually not over ten; and the parasite's body was always exceptionally small. Yet the case was one of tertian fever. A case with indistinct malarial history in a child a little under ten years showed large ring-like parasites with a single chromatin body and large achromatic zone with heavy pigment, in a deeply notched corpuscle, but totally unlike the rings seen in estivo autumnal cases in the crenated corpuscles. Many more instances might be cited. It seems to me that malarial parasites form what one might term involution forms at a time when gametocytes (which I consider an expression of the necessity of sexual reproduction) make their appearance. The parthoginetic impulse exhausts itself and the vitality of the febrigenous forms is lowered. One cannot know how much the production of possible antibodies may have to do with the phenomenon. That such bodies are formed is reasonable to suppose, as cases of immunity exist, and the study of kindred hematozoa (of trypanosoma, for instance) helps to confirm this belief. To-day, the practioner who owns a microscope is as a rule satisfied with the finding of the hematazoon of tertian fever, but the kind and form and characteristics are not usually considered. As soon as all typical forms have been recognized a better understanding of the asexual cycle and gametocyte formation will be reached. If gametocyte formation could be prevented, transmission of malaria from one individual to another by mosquitos might also be prevented, as the perpetuation of the parasite depends upon them; hence, cases containg the more resistant gametocytes would require greater attention and possibly somewhat different treatment than cases of recent infection with immature parasites. The value of positive recognition of mature forms (gametocytes) in tertian fever, therefore, becomes paramount.

Discussion.

Dr. Ewing: I have been extremely interested in the facts brought out by Dr. Goldhorn. I believe that the question of the differentiation of the sexes in malaria is at the present time one of live interest. I have been over much of this ground without, however, getting all the points obtained by Dr. Goldhorn. Some two years ago I thought that I was able to identify the macro- and microgametes, but was not certain because I was not able to follow the cases through a series of paroxysms. Since that time one writer at least has attempted to differentiate the male and female parasites in the blood. Argutinsky, (*Arch. f. Micr. Anat.*, Bd. 59, 1902.) As the malarial paroxysm progresses the morphology changes and the male and female parasites become clearly differentiated. I do not agree in every particular with Dr. Goldhorn's conclusions. In the first place, Dr. Goldhorn found that the male stained lightly with methylene blue; in my specimens the male stained darker than the female, though that was possibly due to some difference in technique. I have always found, as did Dr. Goldhorn, that the flagella are extruded from one point in the microgamete, but before the extrusion of flagella I have sometimes seen the chromatin subdivided into four or six groups.

SEVERAL CASES OF DYSENTERY REFERABLE TO THE BACILLUS OF SHIGA.

W. H. PARK, M.D.

I recently became interested in dysentery while staying at Mt. Desert this summer with Dr. E. K. Dunham and Dr. Flexner. There was an outbreak of a number of cases of dysentery in some of the families living nearby. There were probably twenty cases in all, occurring mostly in children. Dr. Flexner kindly sent to Philadelphia for cultures of the Shiga bacillus so that in case of failure to obtain cultures from these cases they might test the serum reaction. The day the cultures came, Dr. Dunham succeeded in getting serum from two children sick with dysentery and both specimens gave a marked reaction with the cultures from Philadelphia. The same day I saw a case of dysentery and obtained some mucus directly after its expulsion from the rectum. This was plated, and I got the dysentery bacillus of Shiga, which I now show you in the tubes. This bacillus appears to have the same characteristics as those isolated by Shiga in Japan and by Flexner in this country and in the Philipines. I also show you three tubes showing the growth in the Hiss media of the Shiga dysentery bacillus, and of the colon and typhoid bacilli. The dysentery bacillus remains isolated and does not disseminate through the media nor produce gas. The colon bacillus passes throughout the media producing a general cloudness varied by little streaks due to the passage through the media of gas bubbles. The typhoid also passes throughout the media but causes no appreciable gas and therefore leaves no streaks. This investigation made therefore the interesting fact apparent that there was an epidemic in Mt. Desert in which the Shiga bacillus was the exciting factor giving rise to acute dysentery. On my return to the city, I thought it interesting to see how much dysentery was present in New York and how prevalent was the Shiga bacillus. Inquiries made among the hospitals and asylums developed the fact that there was very little dysentery then present in the city. On case, accidentally found, was that of a man who had come from the Philipines three years before, and who ever since had had subacute dysentery. For two or three weeks he would be fairly well, never entirely so, and then he would have an acute attack. His blood showed a marked reaction with the Shiga bacillus, and this bacillus, as well as the amœba coli was found in his stools. This case then seems to be a case a chronic dysentery due to mixed infection with the amœba coli and the Shiga bacillus. Two cases were found, of a man and a baby, who had had dysentery six weeks before and whose blood gave the specific reaction. In thirty cases where the blood from suspected typhoid patients was examined one gave a reaction with the Shiga bacillus. This blood caused agglutination of both the typhoid and dysentery bacilli. The blood of a number of children who had recently suffered from acute entero-colitis did not agglutinate the dysentery bacilli even when used in a dilution of one part of serum to ten of bouillon. This is interesting in view of the preliminary report from Baltimore where the Shiga bacillus was abundantly present in the stools of children suffering from acute entero-colitis.

A SOLITARY TUBERCLE OF THE BRAIN.

DAVID BOVAIRD, M.D.

The specimen which I present is of rather peculiar clinical interest. It was taken from a girl six years of age, whose family history was entirely negative. When first seen, November 29, she gave a history of having had a fall the previous July. The symptoms dated from that time. Two weeks later there was a loss of power in the right leg, and still later in the right arm and right side of the face. On examination there was found to be a paralysis of most of the muscles of the leg and of the muscles of the arm as well. The tongue deviated to the right on protrusion and on smilling the right side of the face showed no action. A diagnosis was made of cerebral paralysis. A brace was applied to prevent the dropping of the leg, but the improvement was not satisfactory and in March she was admitted to the hospital for the correction of the condition in her right leg. Upon her admission her leg was put in plaster of Paris. Finally the child developed symptoms of pneumonia and later gradually developed meningitis. The disease ran the ordinary course of tuberculous meningitis and the child died. At autopsy, the brain was found generally congested. Over the base of the brain there was a thick greenish-yellow exudate. In the sulci, especially along the middle cerebral arteries were multitudes of miliary tubercles. In the left hemisphere, just beneath the upper end of the fissure of Rolando and about one cm. from the surface, was the solitary tubercle, about four cm. in diameter presented as a specimen. Immediately posterior to this was a second mass, about one-half the diameter of the first. Several bronchial glands were tuberculous; one was calcareous. There were scattered areas of bronchopneumonia in the lungs. The viscera was otherwise normal. This case was of especial interest because of the size of the tubercle, which was very unusual for a child of six years—the largest that I have ever seen in a child's brain. The history is interesting as evidence that this solitary tubercle developed as a tumor of the brain and was responsible for the condition found in the right leg, in the right arm, and in the right side of the face, and that the tuberculous meningitis was a secondary development following the child's admission to the hospital. It is the only case of this character that I have ever come in contact with—a solitary tubercle developing in the brain of a child just as a tumor might have done, and during its early stages entirely devoid of any symptoms pointing to its tuberculous nature.

A CASE OF TRAUMATIC DISEASE OF THE AORTIC VALVE.

E. LIBMAN, M.D.

The heart which I present was obtained at the postmortem examination of a man thirty-three years of age, who had succumbed to an infection by a paracolon bacillus. The history of the case in so far as it appertains to the heart was as follows:—There was hypertrophy and some dilatation of the left ventricle. There was a slight systolic murmur at the apex and over the aortic valve. There was a rough systolic murmur over the pulmonic orifice, without visible pulsation. The second sound was louder over the pulmonic than over the aortic orifice. The murmur was not heard in the vessels of the neck. The diagnosis wavered between several conditions. In the first place, the patient had had six children, nearly all of whom had died in early infancy, having been "blue babies". This being taken into consideration, it was thought possible that the patient might have a similar condition, but no one of the usual congenital lesions in itself would very well account for the physical signs present. The possibility of an acute endocarditis due to the paracolon bacillus was also entertained. A lesion of the aortic valve in which the murmur was heard over the pulmonary orifice was the third diagnosis considered. The relatives of the patient stated that he had been perfectly well up to the age of three years, when he was run over and three of the upper ribs on the left side anteriorly, were fractured. After that, a very marked cardiac impulse had been noticed and he suffered from palpitation. It could not be ascertained whether or not fever was present after the injury. The lesion found in the heart is of such a nature that it can only be explained as the result of the traumatism. The anterior and the right posterior flaps of the aortic valve were found torn loose from their attachment to the aorta. There was considerable thickening found at the place from which the flaps were detached, and the two flaps were found to be agglutinated by fibrous tissue with calcareous deposit. Furthermore, there was a line of calcareous tissue running directly across the anterior flap, which also extended down over the endocardium for a distance of about one-half of a centimetre. There was no atheroma of the aorta. One cannot help coming to the conclusion that the trauma sustained thirty years before death had resulted in a tear across the anterior flap of the valve and in a detachment of two flaps from their attachment to the aorta. The question remains open whether the changes found were due in part to an infectious process following the traumatic lesions or not. Prof. Prudden has shown that endocardial changes may result after trauma without the occurrence of any infection.

MIXED TUMORS OF THE PAROTID.

F. C. WOOD, M.D.

Two mixed tumors of the parotid have recently come under my observation. In one of these tumors, which showed a typical endothelial type of growth, there were numerous epithelial pearls containing spine cells. The second case is a tumor of long duration in which flat celled carcinoma developed in the substance of a congenital endothelial tumor.

Discussion.

Dr. Libman: During the past year we have had at the Mt. Sinai Hospital laboratory a case of mixed tumor of the parotid in which we found distinct areas of epithelioma.

A CASE OF GENERAL TUBERCULOSIS.

G. ROPER, M.D.

I present this specimen because of the condition observed in one of the ovaries. The patient was a colored woman, aged thirty-seven years. Seven months previously, after giving birth to her fourth child, she had had a slight cough and expectoration. Two weeks after delivery, night sweats began and she lost flesh and had considerable pain in the abdomen. On physical examination there was found to be a distended mass in the abdomen with considerable fluid. At autopsy the retro-peritonial glands were found to be enormously enlarged and tuberculous. There was also a general miliary tuberculosis of the spleen and lungs. The right ovary was filled with numerous large tubercles. The other ovary was normal. The exact seat of the original lesion could not be definitely determined.

Discussion.

DR. EWING: Were any intestinal lesions found?

DR. ROPER: There were no intestinal lesions. Dr. Biggs had been inclined to think that the pulmonary glands might have been the original seat of the trouble; but they were but moderately involved, while the retroperitoneal glands were enormously enlarged.

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DR. JAMES EWING, *President.*

OBSERVATIONS ON ADRENALIN GLYCOSURIA, AND CERTAIN RELATIONS BETWEEN THE ADRENAL GLAND AND CARBOHYDRATE METABOLISM.

C. A. HERTER, M.D.

The form of glycosuria that is induced by the use of adrenalin preparations resembles in certain respects the glycosurias seen in the human subject. It is a matter of special interest that we should be able to produce glycosuria by the use of a substance derived from certain normal cells of the body. It gives to the subject a physiological interest which does not obtain with many other forms of glycosuria. The history of this subject begins with the first person who called attention to the fact that glycosuria followed the use of suprarenal extracts given subcutaneously. This was F. Blum, who in September, 1901, published observations which indicated that watery extracts from the sheep's suprarenals were capable of inducing glycosuria in dogs and rabbits when injected subcutaneously. The amount of this glycosuria was so slight that it was at first thought that it was not of great interest and but little importance was attached to it; but taking up the subject later and working with adrenal extracts and also with the pure adrenalin furnished by Prof. Abel, of John Hopkins. I was able to work out a number of facts in regard to the character of this glycosuria which are of considerable interest.

In the first place, I found that when doses of from two to five or six c.c, of a one to one thousand solution of adrenalin chloride were introduced into peritoneal cavity of the dog, a very pronounced glycosuria was developed with a percentage of sugar ranging usually from three to ten per cent. This gradually wore off and in the course of thirty hours the glycosuria disappeared. If one gives the dose under the skin the resulting glycosuria is much less well marked. It was also proved that if the dose be given by the mouth, the result is much less pronounced. For example, if one injects into the peritoneal cavity of the dog two or three c.c. of adrenalin, one gets a glycosuria with four to six per cent of sugar. If one takes fifteen or even twenty c.c. and gives it by the mouth to the same animal, there follows either no glycosuria at all or one of slight degree. To a dog weighing about twenty-five pounds it was necessary to give thirty c.c. of adrenalin in this way in order to bring about glycosuria.

The explanation of this is simple and it has a certain practical interest for those who make use of adrenalin in the practice of medicine. Adrenalin is easily oxidized, and exposure to air causes it to change color and to lose its activity. If, however, the oxidation process is carried on more actively, as by the use of chlorine or bromine, it is very easy to quickly oxidize the adrenalin so that it loses both its power to contract vessels and to produce glycosuria. It seems therefore probable that the cells of the stomach bring about an oxidation of the adrenalin which destroys it in large part before it is absorbed. It is preferable on this account to make use of the subcutaneous method. There is no objection whatever to its use in this way and in heart disease, doses of from five to ten grains every three hours give rise to no glycosuria. Intravenously one gets glycosuria also, but it does not seem to be of so high a grade as when the dose is given intra-peritoneally. Moreover, in some of Prof. Abel's experiments he did not get glycosuria in much more than one one-half of the cases. As a rule there was either a good deal or none at all. My own results have been more constant, but glycosuria was not so regularly obtained as in the cases where the dose was given intra-peritoneally. During the glycosuria, which is caused by adrenalin the amount of sugar in the blood is distinctly increased above the normal. This is a regular occurrence. In this respect therefore the adrenalin glycosuria resembles the glycosuria found in the human subject which is almost invariably associated with some rise in the proportion of sugar in the blood.

Another interesting fact brought out is that when applications of the adrenalin were made to the pancreatic gland itself it was possible to call forth a large amount of sugar by means of a small amount of adrenalin applied to the organ, one c.c. for instance. With this dose given intravenously or injected into the liver or directly into the mesenteric vein, one gets very little glycosuria.

I also made several experiments in which the pancreas was repeatedly painted with adrenalin. The results as regards the urine showed large quantities of sugar. In cases where single paintings are given the quantity of sugar obtained is not large; but where the applications are repeated it is very much higher. Under certain conditions the quantity of sugar which can be brought forth is very large; but where the drug is given so that it acts for a few minutes only, a small amount is obtained. Where the effect of the drug can be made continuous the quantity of sugar is simply enormous, as large as in severe cases of human diabetes.

What is the character of glycosuria? How it is brought about? The answers to these questions it is impossible to give fully as yet, but there are certain facts that stand out clearly. In the first place, the sugar we get depends upon excessive conversion of glycogen into sugar. There is no evidence at all that it depends on diminished combustion, at any rate at first. A method has been devised by Dr. Richards through which it is possible to simultaneously remove blood from the femoral artery, the hepatic vein, and the portal vein. In three observations which are quite typical, it was shown that the blood sugar in the portal vein undergoes comparatively little change; the rise takes place very much more slowly than in the hepatic vein where there is a considerable increase. We may conclude therefore that, at any rate in the beginning, the sugar that appears depends upon excessive conversion of glycogen into sugar in the liver.

The next question is: What is it that causes the excessive conversion of glycogen into sugar? To this there is no positive answer, but there are a number of things which make us feel that this change comes about through the medium of the nervous system. My reason for thinking this is, briefly, that if one collects the blood from the pancreatic vein after painting with adrenalin and then injects it into the blood of a normal animal, one gets only a trivial glycosuria. Apparently nothing leaves the pancreas to go to the liver to call forth excessive conversion. Some stimulus occurs to the pancreas which in an obscure way brings about the excessively rapid conversion of the glycogen into sugar.

In my work upon the glycosurias following the use of adrenalin I found it very helpful to study the affect of other substances applied to the pancreas. One of the substances so studied was cyanide of potassium. Seppert showed some years ago that the effect of poisoning with hydrocyanic acid was to deprive the cells of the body of their ability to take up oxygen. He made it very clear also that under certain conditions of poisoning by hydrocyanic acid the cells are not able to take up oxygen from the arterial blood and therefore the blood circulates without losing its oxygen. Observations made upon the content of the oxygen in the arterial blood and in the venous blood showed this contention to be very well founded. This fact helps us when we come to study the adrenalin glycosurias, because when cyanide of potassium is applied to the surface of the pancreas it is possible to bring about glycosuria, though usually very slight. When one applies or injects the same quantity of potassium cyanide into other organs one does not get a glycosuria. Moreover, one can inject into the blood very considerable quantities of hydrocyanic acid without getting any glycosuria. This is an elemental point in the work. (Dr. Herter exhibited tables showing the effect of applying potassium of cyanide to the pancreas.) In this work I used a one thousandth normal solution, generally one or two c.c., either applied to the surface of the pancreas by painting or injectiug into the substance of the organ. In one case I obtained 2.1% of sugar; in another, nothing; in another, a trace; again, nothing; in another, 1.5%; in two cases, traces. Out of about one dozen cases in which I gave injections of the same quantity or of very much larger quantities (ten, one hundred, or two hundred and fifty c.c.) of a one hundredth normal solution all were absolutely negative. The injections into the mesenteric vein were entirely negative. The importance of this fact is that it shows that the action of the cyanide when it is applied to the pancreas seems to be local. If the pancreas is cut into two and the poison applied to one end we can be pretty sure that it does not act upon the other end. It is not carried around by the blood. Therefore, if we get a glycosuria from painting one end of the pancreas we have a condition which affects that end only and there is no reason to suppose that the other end is similarly involved. This being the case with cyanide of potassium, it becomes likely that it is the same in the case of adrenalin glycosuria.

Observations were made with a variety of substances in order to see what sort gave rise to glycosuria and what sort did not. Of course, it was not possible to make generalizations in regard to a large number of substances, since one substance alone requires the sacrifice of a large number of animals. The action of the adrenalin on the pancreas is hinted at by the action of hydrocyanic acid and potassium cyanide, which set up a slight glycosuria. Sulphurous acid, carbonic oxide, benzyl alcohol pyrogallol, and pyrogallol are reducing agents and act powerfully on the pancreas. The common oxidizing agents gave results very different. Nitric acid, hydrogen peroxide, chlorine, bromine, and osmic acid all gave negative results. The only oxidizing agent which was found to produce glycosuria was nitrobenzol, but there are doubtless others. Sodium salicylate brings out large quantities of sugar. Sodium thiosulphate is negative. It is clear enough, therefore, that the mere reducing power does not explain the action of these drugs; but it is interesting that they seem to be more likely to produce glycosuria than the ordinary agents. That fact in connection with the action of the cyanides led me to put forward the suggestion that the glycosurias obtained by the application of adrenalin to the pancreas depend upon interference with oxydations in the pancreatic cells.

Opie found that the tail of the pancreas contains a somewhat larger number of islands of Langerhans than the head. It occurred to me that it would be of interest to see whether there was any difference in the action of the adrenalin on the head and tail of the pancreas, and on this point I made a number of experiments. The pancreas was cut into two parts. The head or tail was then painted with adrenalin, either one or two c.c. for about ten minutes. Observations were made on thirty dogs treated in this way, and the results while not at all conclusive were not without a certain amount of interest. In fifteen observations in which the head was painted first the total amount of sugar was 15.6 grammes; whereas in fifteen observations in which the tail was painted first, 17.25 grammes of sugar were obtained. This shows a little in favor of the tail, but it is of course not conclusive.

Since these investigations I have made observations on the suprarenals in order to see whether there was any relation between the suprarenals and the occurrence of glycosuria. Four things were observed which led to the opinion that the suprarenal gland influences carbohydrate metabolism in an important way. One is that intermittent massage of the suprarenals was followed by glycosuria. Another is that extirpation of both adrenals was followed by a fall in blood sugar. The third is that adrenalin failed to induce glycosuria when injected intraperitoneally into dogs from which the adrenals had been previously removed or in which the adrenal vessels had been tied. Finally it was found that the onset of glycosuria after extirpation of the pancreas is delayed by previous extirpation of the adrenals. This inhibitory effect is only temporary. I at first interpreted these facts as meaning that the phenomena observed are due to chemical derangements connected with an excess or diminution of an adrenal internal secretion. It now seems likely that many of the phenomena are really of nervous origin and further work is necessary to decide whether the internal secretion hypothesis is tenable, and if so, to what extent.

Discussion.

DR. EWING: I feel that these studies furnish a very large amount of information on the subject. I would many times have liked to stop Dr. Herter to ask questions, make suggestions, and put various queries. I felt that a paper of this sort could be discussed only at great length and only by those who are intimately familiar with the subject; and that, therefore, the amount of discussion which such a paper would bring forth must be totally inadequate to the value of the paper. It seems to me that if Dr. Herter had succeeded in showing that an injection of adrenalin extract produces glycosuria; that the application of the substance to the surface of the pancreas produces glycosuria; that compression of the adrenal gland produces glycosuria, while compression of other abdominal structures does not; that tying off the vessels of the adrenals renders it impossible to produce glycosuria by ordinary means; that if, after extirpation of the pancreas, the glycosuria is diminished by tying off the adrenals, he has a considerable volume of evidence to show that the adrenal is very important in the pathology of human diabetes.

DR. HERTER: I realize very well that unless the members of the Society had a chance to think over the facts brought out it is unsatisfactory to enter into a discussion. I feel sure that the facts will stand the test of subsequent observations but as to the construction to be put upon them I cannot speak confidently. It looks to me as though it were safe to assume that the suprarenals exert a marked influence on carbohydrate metabolism. I was at first inclined to put a chemical construction on all the facts, but on more careful consideration have come to the conclusion that I was not justified in doing this without further data. I believe my experiments should show whether or not the blood passing through the pancreas is in any way changed so that its sugar is converted into something else in preparation for the process of storing in the liver. The study of carbohydrate metabolism is very complex. There can be no doubt that all active metabolism of the body is closely connected with sugar combustion. More than one-half of the energy of the body comes from sugar. The question is not limited to the pancreas or adrenals or nervous system. It is something that concerns every tissue in the entire body.

A MELANOMA IN THE COW.*

V. A. MOORE, D.V.S.

The case was one of great interest on account of the extent of the tumor growth. There was no history. The growth was primary in the breast, there being a very considerable mass of tumor in that region. The exact location could not be made out, but on the skin there were a few pigmented spots from which the original growth may have sprung. There was a very large mass in the udder which measured ten by six by five inches. The center was softened. From this starting point all the viscera of the animal were extensively affected. The liver was very large and showed very distinctly the relation of the tumor to the liver parenchyma. A most interesting feature was the manner in which the growth passed along the superficial lymphatics of the diaphragm. At the tendinous edge there were several large cauliflower masses, very densely pigmented; while along the tendinous fibers were thin elongated masses, coal-black in color, apparently distending the superficial lymphatics. The heart was riddled with small nodules of melanotic tumor. Beneath the periosteum of the ribs there were large diffuse tumor masses. The microscopical structure was similar to that which is seen in the human subject. The cells in the secondary growths were almost all fusiform and richly pigmented. The original point of development was not found.

Discussion.

Dr. Ewing: I am inclined to accept the belief of Unna, Marchand, and others, that these tumors are, in a large majority, epitheliomata arising from the basilar cells of the Malpighian layer of the skin and showing very atypical cell forms in the metastasses. In a series of melanomata I have found some which showed very distinctly that the beginning of this process was well within the epithelial layer of the skin, from which foci there was a proliferation of the cells into the derma. From this point the cells become atypical and epithelial characters are not retained.

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* This report was presented for Dr. Moore by Dr. James Ewing.

DR. GEORGE P. BIGGS: The presentation of this case has been extremely interesting to me, particularly the remarks on the nature of these growths. I have come to the same conclusion as the result of a specimen examined where the growth was studied in early development. There were very clearly shown in some places branching columns of epithelial cells working down into the deeper tissues, and the tumor as a whole had an alveolar arrangement. I diagnosed the case as of epithelial origin. The tumor had originally occupied the outer surface of the arm, and the metastases removed several weeks later from the axilla had the appearance of pigmented embryonic connective tissue growths; but taking the primary lesion into consideration, one was forced to the conclusion that these irregular cells of the secondary deposits were also of epithelial origin.

DR. EWING: The name melanoma was used by Virchow who gave it in order not to define his position more fully. I have recently been shown some sections of embryonic eyes in which the pigment cells of the choroid could be demonstrated as continuous with the retinal epithelium and therefore evidently of epithelial origin. This relation, however, is denied by most opthalmologists. One of the chief arguments against the epithelial origin of melanomata has been that very similar tumors are found to develop from the "connective tissue" cells of the choroid. It will be seen, however, that if the choroid cells themselves are derived from epithelium the argument loses one of its chief supports.

A CASE OF QUARTAN MALARIA, WITH DEMONSTRATION OF SPECIMENS.

F. C. WOOD, M.D.

I called the attention of the Society to the specimen because in my experience these cases are exceedingly rare in New York. I personally have never seen a case before; the specimens which I had seen were obtained through the kindness of the John Hopkins Hospital Staff.

The patient was an Armenian, about thirty-five years of age, who had been in New York for the past two years. While in Asia Minor he had suffered for several years with irregular attacks of fever. During his residence in this city he had also had attacks of fever at irregular intervals, the attacks lasting usually for two or three weeks and being then followed by a period of comparative health. He has taken quinine but without the supervision of a physician. The present attack had lasted for about three weeks. The patient had a chill regularly every fourth day, beginning at eleven o'clock in the morning. He had an enlarged spleen and very marked anaemia, the hemoglobin being about fifty per cent. The blood at the time of the beginning of the chill showed very beautifully the characteristic rosettes of the quartan parasite. None of the rosettes seen had more than nine merozites. In fresh blood the morphology was even better than that in smears and the segmentation was watched a number of times on a warm stage. Very marked phagocytosis was present under these conditions; but there was no evidence of flagellation, though there were a considerable number of gametes in the specimen. The patient was watched through two complete cycles and it was found that there was only a single group of organisms.

The preparations were stained with the Wright modification of the Jenner stain which has in my hands proved a very useful method of staining the chromatin of malarial parasites, though the results were not as perfect as those obtained by the use of the Nocht method. By this chromatin stain two types of gametes could be made out, one form in which the chromatin was collected into small masses in one portion of the parasite; and the other in which the chromatin was in the form of fine dust-like particles. In the presegmenting forms double rods of chromatin in each segment were easily seen, just as has been figured by the Italian observers. Occasionally the red cells showed degeneration, but the cells harboring parasites showed none of the peculiar degeneration which is so frequently seen in cells infected with the tertian organism. In this case all infected cells were small and dark, in contrast to the large swollen red cells of the tertian infection. There was a relative increase in the large lymphocytes, but no other changes were noticed in the white cells.

Discussion.

Dr. Ewing: I consider this specimen a very beautiful demonstration of quartan rosettes, and one that a New York observer very rarely encounters.

A CASE OF MIXED QUARTAN AND ESTIVO-AUTUMNAL MALARIA; A MENINGOCELE.

JAMES EWING, M.D.

This case is presented because of its great rarity, it being the first case of quartan infection that I have seen in a ten years' study of malaria. The patient was a man who had been sent to British Guiana in July, 1902. He returned in September, broken in health, with a history of irregular illness without distinct chills. No distinct chills occurred during the time he was under observation in New York, which was for about a week. A few typical quartan parasites were found in the blood smears and in a subsequent review of the slides crescents were found. We must therefore class this case as a mixed quartan and estivo-autumnal malaria.

The second case is presented for Dr. Otto H. Schultze. It is a specimen of meningocele which was obtained from a child whose body had been taken to the Morgue, and in which the the protrusion included almost the entire cerebellum.

Discussion.

DR. GEORGE P. BIGGS: Quartan malaria is very rare in New York, and I have never been able to convince myself that I have really seen a case.

DR. HARLOW BROOKS: About two years ago I saw a similar case in which the meningocele contained the greater part of the right lobe of the cerebellum and a small portion of the left lobe. The mass had been removed surgically. The child lived for nearly a month after the removal and finally died of pneumonia. The mental status was very low. He was probably idiotic, but as he was but four months old this could not be definitely determined. At the autopsy a condition was found similar to that shown except that the cerebellum was almost completely removed.

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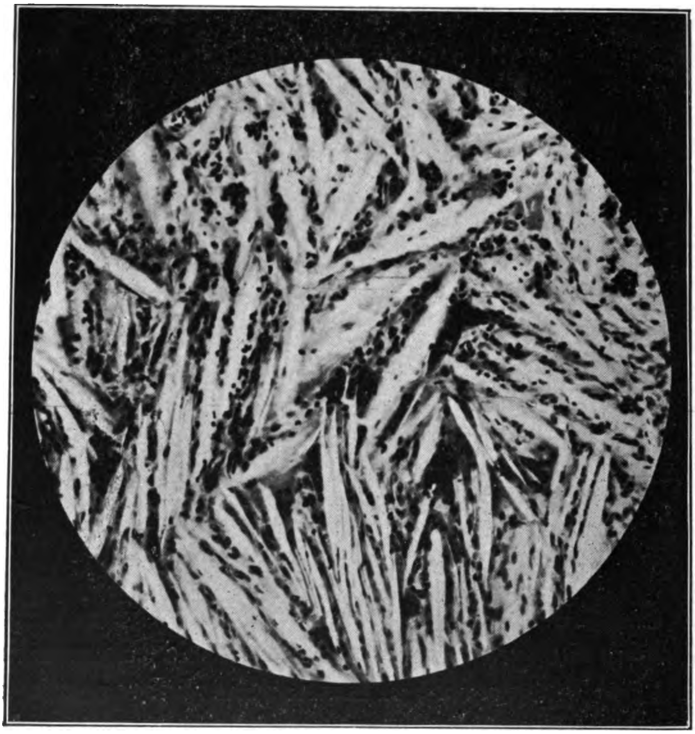
Dr. James Ewing, *President.*

CHOLESTERIN GIANT CELLS.

F. S. MANDLEBAUM, M.D.

In a recent article by Le Count the statement was made that the slits or clefts formed by the solution of cholesterin in granulation and necrotic tissue tumors, formed in the processes of fixation, have frequently been observed and their connection with cholesterin crystals recognized. Le Count says, moreover, that all persons working along general pathological lines are thoroughly familiar with this condition and its occurence is well known to those who make routine examinations of pathological material. In tissue work along these lines during the past twelve years I have met this condition in but two cases and I consequently deem the matter of sufficient importance to bring before the Society. Incidentally I may remark that all the text books with which I am familiar fail to mention this condition.

The first case was that of a woman of thirty years of age who had a small, probably congenital, pre-thyroid cyst. She was operated upon and a small piece of tissue sent to me for examination. The cyst wall had a granular, honey-combed appearance, and was covered with an exudate, the character of which was not known. Several small openings were seen in the deeper parts which barely admitted the end of a small probe.



The second case was a cyst of the breast in a woman of fifty, who had had the condition for ten years. Recently the cyst began to enlarge and a sinus formed which discharged a thick yellow fluid. The cyst was removed and a portion of it submitted to us. It showed the following gross appearances: From the cyst wall there sprang a rather shaggy, dark reddish colored exudate somewhat granular and friable in character, not very adherent to the cyst wall and easily separated from it and measuring from one-half to one cm. in thickness. The nature of this exudate was not recognized. Sections of this cyst and also of the first case showed the following conditions: The first thing noticeable was a large number of slit-like openings, elliptical in shape, pointed at both ends, and very sharply defined, which looked as though they had been punched out of the tissue with a sharp instrument. The next thing noticeable was the large number of giant cells scattered throughout the whole section. They were of the kind generally seen in inflammatory processes, very large in size and containing thirty or forty nuclei scattered throughout the cell body. They were rich in chromatin and stained very deeply. Within the body of many giant cells these small elliptical slits were also noticed. In some there were two such clefts. The rest of the tissue was made up of inflammatory tissue, vascular and connective tissue. Many of the giant cells contained coarsely granular pigment.

A study of the sections proved that these slit-like openings were produced by cholesterin, which in tissue does not take the tablet form usually seen in fluid exudates, but appears in these elliptical shapes. My impression is that the cholesterin was present in combination with fatty acids. The specimens naturally went through alcohol and ether which extract the cholesterin. This explains why one does not discover the cholesterin crystals themselves which are in the tissue, but simple the clefts out of which they are extracted. The alcohol is usually thrown away so that chemical tests cannot be made of it. I nevertheless made such tests but did not get any reaction for cholesterin. I then took a bit of tissue from the second case and macerated it with chloroform and from this solution obtained crystals which resembled those of fatty acids. These crystals and also bits of the tissue itself gave reactions for cholesterin. There was the usual play of colors when treated with sulphuric acid and ferric chloride and the violet color remained. One would imagine that these cholesterin crystals ought to present the familiar appearance described; they do not, however, as many complex changes undoubtedly occur, due to various chemical unions.

I have here sections of both cases and also slides showing the fatty acids obtained by evaporating the chloroform in which parts of the specimen had been macerated.

Thoma, in *Virchow's Archiv*, Vol. CV, reports a case of atheroma of the aorta in which these crystals were found. Also Manasse, in Vol. CXXXVI, gives a number of cases of chronic otitis media, several presenting a similar condition. Carl Meyer, *(Ziegler's Beiträge, 1893*, Vol. XIII), reports the case of an adenomatous cyst of the ovary which ruptured intra vitam, in which at operation a large number of miliary nodules were found scattered over the peritoneum. The diagnosis of miliary tuberculosis was made. Upon microscopic examination the nodules were found to be made up of giant cells and cholesterin crystals. The illustrations which accompany the article are identical with the sections in the present cases. Le Count reports a case of carcinoma of the scalp and a case of a tumor mass removed from the scrotum, in both of which specimens of cholesterin giant cells were found. He also produced similar histological pictures by injecting into the back of a guinea-pig a sterilized salt solution containng pure cholesterin crystals, and by making sections of the nodules which resulted. His article is published in the *Journal of Medical Research*, *1902*, Vol. VII.

Discussion.

DR. WOOD: Has Dr. Mandlebaum made tests on other sections so as to eliminate the possibility of these color reactions having been produced by the action of the strong acid on the proteid of the specimen itself?

DR. MANDLEBAUM: I have not made such tests and I do not know whether the ordinary proteid would give that reaction in strong sulphuric acid and whether that obtained could be due to it. I have made other tests with sulphuric acid and the addition of small quantities of iodine and obtained both reactions. I am inclined to believe these were conclusive. I also evaporated the extracted chloroform and so obtained a reaction. It was not quite so marked with nitric acid and ammonia tests.

THE INFLUENCE OF NEPHRECTOMY UPON ABSORPTION.

S. J. MELTZER, M.D., AND WILLIAM SALANT, M.D.

The object of this research, as the title indicates, was to investigate the behavior of absorption after nephrectomy—a subject which was never investigated before. The fact that œdema, which is an accumulation of lymph within the tissue spaces, is found in many cases of kidney disease, that is, in partial impairment of kidney function, led many writers to the expressed or implied belief that nephrectomy ought to diminish the power of absorption of lymph from the tissue spaces. It must be stated, however, that impaired absorption was left out in the consideration of the well-known theories of œdema. Thus, according to Bright, hydremia is the cause of œdema. Grainger Stewart and Bartels consider hydremic plethora as the cause, while Cohnheim held that increased permeability of the blood vessels brings about this pathological condition. In all of these theories, therefore, increased transudation from the blood vessels into the tissue spaces is considered as the cause of œdema. Not until very recently did it occur to investigators that it might be due also to diminished absorption. As far as we know, Reichel was the first investigator to urge that impaired absorption might account for œdema. He performed a number of experiments on healthy persons and on cases with nephritis or cardiac disease, in whom he injected subcutaneously normal salt solutions. Reichel states that while in the normal individuals the artificial œdema disappeared after two days, it lasted five, eight, and even ten days, in his patients with nephritis or cardiac disease. But Reichel selected cases in which there was no œdema. If his theory be correct, if the formation of œdema be due to impaired absorption, his cases in whom diminished absorption was proved experimentally should have developed œdema. It occured to us that a study of absorption in nephrectomized animals might throw some light on the causation of this pathological condition. Following Reichel's example, we injected subcutaneously into rabbits normal salt solutions, but as absorption by this method could not be studied with any degree of accuracy, our studies were made on absorption from the peritoneal cavity—a method which is capable of giving more precise results. We began by injecting a 0.8% salt solution which we allowed so remain in the peritoneal cavity for from one-half to nineteen hours. Injection was begun immediately after nephrectomy. Since we know that removal of the kidney leads to plethora and consequent increase of filtration, we expected in common with many others that absorption would be better in normal than in nephrectomized animals. In the first few experiments, however, we obtained entirely different results. Absorption was markedly better in nephrectomized than in normal rabbits. We found that the average per cent of absorption per kilometer of normal rabbits was forty-three per cent, while in the nephrectomized rabbits it was sixty-five per cent.

At this stage of our investigation it occurred to us that there might possibly be a rise of osmotic pressure in the blood of nephrectomized rabbits, for the removal of the kidneys which leads to plethora may likewise cause an accumulation of salts in the blood since the osmotic pressure of the urine is normally higher than that of the blood. If this hypothesis be true, 0.8% sodium chloride is no longer isotonic with the blood of nephrectomized rabbits, but is hypotonic.

With this hypothesis in view, several series of experiments were performed with salt solutions of different concentrations, injecting them immediately after nephrectomy or about twenty to twenty-five hours later. The results are as follows:

One per cent solution injected twelve to twenty-seven hours after double nephrectomy: Remained in the peritoneal cavity one and one-half hours. Two experiments. Absorption in normal rabbits = 18% in one; in the other sixty per cent more was recovered than was injected: in nephrectomized rabbits, absorption equalled forty-seven per cent and forty-three per cent; or an average of 21% for the normal to 45% for the nephrectomized rabbits. The next series was experimented upon with 1.2% salt solution, which was injected either immediately after double nephrectomy or from seventeen to forty hours later, and was allowed to remain in the peritoneal cavity one-half to six hours. In eight experiments of this series the average of absorption was one-half per cent per kilo of normal rabbit to twenty-five per cent of nephrectomized rabbit. Our assumption that there is a rise of osmotic pressure in nephrectomized rabbits is made still more probable by the results of our series with 1.5% salt solution. In three out of four experiments we recovered from the normal rabbits from ten to twenty per cent more fluid than we injected, while in the nephrectomized rabbits thirty per cent per kilo was absorbed. In our next and last series with 2% salt solution, negative absorption, that is more fluid was recovered than was injected, manifested itself for the first time in nephrectomized rabbits. In two experiments in which the solution remained in the peritoneal cavity for one and a half hours, five per cent more in one, and twelve per cent more in the other were recovered than injected, which is in all probability an indication that 2% salt solution is hypertonic for nephrectomized rabbits. We wish to add that in experiments with a stay of six hours in the peritoneal cavity there was hardly any difference of absorption between normal and nephrectomized rabbits in any of the different series we considered. We obtained similar results with 2%, 0.8% and 1.2% salt solutions which is apparently due to the fact, experimentally proven by Heidenhain and Orlow, Hamburger, and others, that after a longer stay in the peritoneal cavity liquids, whether hypertonic or hypotonic, become isotonic with the blood. The essential results we obtained are that the power of absorption is considerably increased in nephrectomized rabbits. This holds good for at least twenty-four hours after nephrectomy. We have obtained a positive result in one animal when the fluid was injected forty-one hours after nephrectomy. In another rabbit the results differed and it is impossible to tell whether it was due to the weakened condition of the animal which consequently makes the result obtained under these circumstances doubtful. Our results now explain the fact which has been a puzzle to many experimenters, namely, that no œdema is seen after nephrectomy in animals explain the well known clinical observation of anuria persisting for many days without leading to œdema. The cause of all this is that the first effect of nephrectomy is not an increase of transduation of lymph into the tissue spaces, but an increase of absorption from them.

Discussion.

Dr. Levene: I should like to ask, whether Drs. Meltzer and Salant have considered that there was only the one possibility that the increases of osmotic pressure in the blood was the cause of the impairment of absorption after nephrectomy, and if this was the case and since the discovery was so new, whether there had not been some chance to prove that the osmotic pressure of the blood was really so much higher than in normal animals. It seems to me that in advancing such a new theory it would be desirable to corroborate it. The technical methods of determining the osmotic pressure of the blood are are so simple and easy to carry out that I believe this determination should have been made before such an important conclusion was drawn from the experimental results.

Dr. Meltzer: The experiments were carried out with the idea of demonstrating whether absorption was increased or diminished in nephrectomized animals and the question of the determination of the osmotic pressure of the blood is an entirely secondary matter. Indeed, these determinations have already been made by Koranyi and were published in one of his articles, although as the reference was in a footnote it might easily be overlooked. Indeed, Dr. Salant and myself had not known of it until after we had made some of the experiments. Koranyi states he found a distinct difference in the freezing point of normal and nephrectomized animals. In normal animals the freezing point was 0.56 and in nephrectomized animals, 0.70.

Dr. Levene: I should like to ask if the alterations in the circulation or vasomotor disturbances due to the operative technique might not have caused the increased absorption.

Dr. Meltzer: There was no hyperaemia of the peritoneum after operation. The incisions were made as small as possible and the autopsies showed that there was no peritonitis. Indeed, peritonitis will not favor but rather retard absorption. That there occurs no especial change in the circulation after nephrectomy has been shown long ago by V. Limbeck.

DEMONSTRATIONS OF CULTURES OF THE MENINGOCOCCUS AND MICROCOCCUS CATARRHALIS.

H. L. CELLER, M.D.

During the past five years we have had the opportunity of investigating at the laboratory of Mt. Sinai Hospital, about twenty cultures of the diplococcus intracellularis of Weichselbaum. A review of the literature on this subject demonstrates that considerable confusion concerning the characteristics of this organism exists. Our results on the other hand, with the exception of slight and unimportant variations, have been constant and agree in all essentials with those of Weichselbaum and his assistants. (Ghon and Albrecht, *Wiener Medizinische Wochenschrift, 1901.*)

Morphologically the meningococcus appears as a diplococcus, the contiguous sides of the individual members being flattened and separated by a fine line of division appearing as an unstained area under the microscope. There is a marked tendency to form tetrads, but the chain formation described by Heubner, Jaeger and others, we have never seen. It is common to find great variations in the size of the individual cocci, large forms appearing next to small ones, especially in older cultures. All of our cultures were invariably decolorized by Gram's solution; we have never met with the non-decolorizing form of Heubner. The organism shows no capsule.

Growth on agar is not constant. Some of the cultures grew upon this medium at first but later lost this power, while others showed a gradually increasing profuse growth and could readily be kept alive by transplanting to fresh tubes at intervals of a few days. The addition of human serum—ascitic, pleural or hydrocele—to the agar always gave better results, but the most luxuriant growth was obtained upon the medium devised by Dr. Libman, serum agar plus glucose (½ to 2%). Maximum growth was obtained with the higher percentage of glucose. With the addition of still higher percentages of glucose (3, 4, 5%) as well as with the use of lactose of sacharose (2%) the development of the organism was neither furthered nor hindered. On Loeffler's serum there is an abundant growth, but there is no advantage over the serum glucose media just described. On glycerine agar the growth varies, usually only a few fine colonies being obtained; but on the addition of serum the growth is profuse.

In fluid media the organism grows characteristically. The growth begins as a diffuse cloudiness near the surface that after two or three days forms a white scum on the surface. The remainder of the medium is at first clear, later slightly clouded, while at the bottom of the tube there is a floccular sediment. There is considerable difficulty in obtaining growth in this form as the shaking of the tube will prevent the formation of the scum or cause it to break up and fall to the bottom after it has formed

The majority of our cultures have grown slightly in ordinary bouillon with and without the addition of sugar in the form of glucose, lactose, or saccharose. Some, however, have only grown upon the addition of serum; the sugar in these cases having apparently little advantageous effect. There is no gas formation in these media in Smith fermentation tubes in which growth is confined to the bulbs.

In litmus milk we have been able to demonstrate growth. The milk is not coagulated and there is no acidity production. On gelatine there is no growth at room temperature.

On potato the results have varied. Sometimes there is no growth, while at others there is a delicate film on the surface that is seen with difficulty or can only be demonstrated by spreads made by scraping the surface of the medium.

Anaerobically there is no growth.

Almost identical morphologically with the meningococcus, but differing from it culturally, is another organism found in normal and some in pathological conditions on mucous membranes of the respiratory tract, in the eye, the ear, and occasionally in the urethra. This is the micrococcus catarrhalis of Ghon. Our culture of this coccus, obtained through the courtesy of Dr. Buerger of the German Hospital, was isolated from a throat culture.

In spreads this organism also appears as a diplococcus, with some flattening of the adjacent sides of the individual cocci. It decolorizes with Gram's solution. There is no capsule. In all its characteristics it bears so close a resemblance to the gonococcus that it can be differentiated therefrom under the microscope only with great difficulty. The tetrads formed by meningococcus as well as the large forms already described will sometimes, however, serve to differentiate this from the other two organisms. Further, the individuals of the micrococcus catarrhalis are more nearly oval than those of either the gono- or meningococcus.

On agar the micrococcus catarrhalis grows profusely, even in the first generations, herein differing from both the meningococcus and gonococcus, that show either no growth or very slightly growth on this medium. The use of glycerine or serum agar, Loeffler's serum or Libman's serum media affords no particular advantage. In fluid media the scum formation already described is readily obtained if the cultures are not disturbed. The membrane lacks, however, the homogeneity of that formed by the meningococcus, being composed of dry granular clumps floating on the surface. In the variation in the cloudiness of the medium as well as in the flocular sediment, the two organisms are identical. There is no gas formation in glucose, lactose, or saccharose bouillon in fermentation tubes; growth is confined to the bulb. Unlike meningococcus, acid production in glucose and saccharose bouillon is demonstrable.

In litmus milk there is growth without coagulation or acidity production. On gelatine there is no growth at room temperature, but Ghon reports slight growth after five or six days under proper thermal conditions. On potato, growth is fairly luxuriant, older cultures appearing yellowish brown; the water remains clear. Anaerobically there is no growth.

On plates the meningococcus and micrococcus catarrhalis are readily differentiated. The superficial colonies of the former are light brown in color; there is no nucleus, but at the center are large clumps that gradually diminish in size toward the periphery. The outer zone is finely granular and paler in color. The edge is sharply defined, circular and regular. There is a very close similarity between these colonies and those of the gonococcus. The colonies of the micrococcus catarrhalis are dark brown in color, lighter at the periphery. The older colonies show a distinct dark nucleus, the remainder of the colony being finely granular. The edge is sharply defined and circular but differs from that of the meningococcus in being irregular as though gnawed. Macroscopically the nucleus of the colonies of micrococcus catarrhalis and the white lacquered surface as compared with the absence of nucleus and the grayish-white surface of meningococcus colonies will serve to distinguish between these two organisms.

A most important means of differentiation is furnished by the nature of the growth both on slants of solid media and on plates. On the former the meningococcus presents a shining greyish moist growth that is viscid, stringy and readily scraped from the surface. The growth of the micrococcus catarrhalis, on the other hand is white, dry, crumbly like mortar, and adheres to the surface of the medium. Sometimes the entire growth may be removed as a membrane. On plates the same differences are seen. The viscidity of the meningococcus colonies stands in marked contrast to the dryness of the colonies of micrococcus catarrhalis, that slide along the surface of the medium without breaking up.

It is impossible to enter here fully into the further questions of the influence of titre on growth, and of pathogenicity. Regarding the latter, our results agree with those of other investigators. Our experiments have been limited to inoculations into white mice, guinea-pigs and rabbits. Subcutaneously both organisms are without effect. In a small proportion of cases intraperitoneal and intrapleural inoculations of either meningococcus or micrococcus catarrhalis in mice and in guinea-pigs have been fatal. Autopsy shows a sero-fibrinous peritoneal and a haemorrhagic pleural exudate. A splenic tumor may or may not be present. All the viscera show hyperaemia and degeneration. The organism may be recovered from the exudates and sometimes from the blood and spleen. The virulence of the micrococcus catarrhalis is far less marked than that of the meningococcus. Larger animals are less susceptible. In rabbits, howeverr, intravenous (Ghon, Weichselbaum) and intracranial (Weichselbaum) inoculations of the meningococcus have proven fatal. Injections into the meninges of goats with the production of meningitis have been successfully carried out both by Heubner and by Councilman, Mallory and Wright.

REMARKS ON THE MENINGOCOCCUS AND ON ITS RELATIONSHIP TO THE GONOCOCCUS AND MICROCOCCUS CATARRHALIS.

E. LIBMAN, M.D.

In connection with the demonstration by Dr. Celler, I should like to make some remarks on my experience with the meningococcus, particularly with the idea of attempting to throw some light on the questions in dispute. During the past five years I have had the opportunity of studying bacteriologically over one hundred cases of meningitis. In most of these, the fluid obtained by lumbar puncture intra vitam was examined; in a few, examinations were made at autopsy only. In these cases I have had the following results:—

Tubercular cases	44
Streptococcus cases....	17
Pneumococcus cases	6
Staphylococcus aureus cases.......	3
Pseudo-influenza bacillus cases	1
Proteus vulgaris cases	1
Bacillus pyocyaneus cases....	1
Diplococcus meningitis cases	20

In a few cases, streptococci and a variety of bacilli were found; the last could not be grown aerobically. I suspect that these were anærobes, particularly as all these cases were secondary to mastoid disease. These cases occurred in all the services of the hospital; a few are cases in the private practice of other physicians and myself. (The larger number of cases due to the meningococcus occured in Dr. Koplik's service.)

I wish now to state our opinions on several mooted points, based on a study of these cases. I shall be very brief, as I hope to report on these data in full on another occasion.

1. As to the relationship of the pneumococcus and the meningococcus from an epidemological standpoint. All our pneumococcus cases were secondary. Observations recorded in the literature would seem to indicate that the pneumococcus can cause epidemic meningitis. Of course, most of these reports were made at a time when the organisms under discussion were much confused. Further observations are neccessary. It is to be noted that any pathogenic organism may produce a meningitis as the only evidence of a systemic sepsis; and an organism may cause a meningitis by first causing an otitis media or a small area of pneumonia. If the primary disease leads in a short time to a meningeal inflammation, the case clinically corresponds to a primary meningitis. One of our pneumococcus cases was characterized by an acute meningitis following within less than twenty-four hours an apparently mild otitis media without pus production.

2. There are on record descriptions of a number of varieties of the meningococcus (Heubner, Jaeger, and others). Some correspond to what Weichselbaum described. Others differ in holding the Gram stain, in the profuseness of their growth on ordinary agar and bouillon or in their growth on gelatin media, etc. All our cultures corresponded to those described by Weichselbaum. None of them ever showed Gram-positive diplococci. There is a variation in the growth on media not containing serum; but when we obtained growth on these media it was never profuse. We only once obtained a growth (very slight) on gelatin at room temperature, and hardly any or none on potato in the incubator. According to

our experience then, there is but one type of the diplococcus meningitidis in the New York cases of cerebrospinal meningitis. Councilman and Wright found the same in Boston, Osler and Hirsch in Baltimore, and Herrick and others in Chicago. We are inclined to believe that there is but one type of organism at play in the European cases. The description of other varieties we believe to be due to one of three causes:—

a) Variations in the use of the Gram stain;

b) Use of other methods for differential staining. (For instance, Heubner uses a Gram-Weigert stain.)

c. The occurrence of skin contaminations (staphylococci).

3. If it were not for a statement in Leube's book on diagnosis (last edition), it would hardly be necessary to point out that the pneumococcus should not be confused with the meningococcus. Leube says that animal experiments are necessary for the identification of these organisms. However, if it be granted that the meningococcus does not hold the Gram stain we have a fundamental difference. Furthermore, the pneumococcus is lancet-shaped, has a capsule, diffusely clouds bouillon, grows much less profusely than the meningococcus in serum media, etc.

4. As to the occurrence of the meningococcus in the nose and throat, we have made no extensive observations. We found several years ago that other diplococci occur in the nose and throat which resemble the meningococcus morphologically and in staining reactions. In one case, reported by Dr. Koplik in the *Medical News* of last year, Dr. Schwarz found the meningococcus (proven culturally) in a conjunctival inflammation which was followed by a fatal attack of meningitis. The

meningococcus was repeatedly found in the cerebro-spinal fluid.

5. The demonstration of the micrococcus catarrhalis by Dr. Celler I consider of prime importance not only with regard to the undoubted confusion it has caused with regard to the meningococcus, but also because it can be so easily mistaken for the gonococcus if cultures are not made. I have repeatedly seen it in cultures from the throat and in sputum, and once in otitis media. It has been found in the urethra, and probably in the conjunctival sac. The culture of the micrococcus catarrhalis demonstrated to-night corresponds to those which Ghon and Albrecht describe (*Zeitschrift für Klinische Medizin*, Vol. 44). I am convinced that this is but one of a group of closely allied organisms. Dr. Celler has detailed sufficiently how easily it is to be distinguished from the meningococcus.

6. Dr. Celler's remarks have also indicated how the meningococcus can at times closely resemble the gonococcus culturally. It is important to differentiate the organisms carefully. This is true not only from a mere technical standpoint but also because the question may arise clinically. Thus, Fraenkel has described meningococcus-like organisms in conjunctivitis. Furbringer reported a case in which a cerebro-spinal meningitis occurred in a patient with gonorrhoea. The meningococcus was found in the puncture fluid and apparently (cultures not made) the gonococcus in the urethral discharge. Furthermore, there are reported two cases in which the meningococcus was found in the blood; in one, long before symptoms of meningitis were manifest. In such cases as this last, careful methods should be used before the identity of the organism is established. We would lay special stress on these points:—

A. The occurrence of tetrads and the irregularity in size and staining reactions of the meningococcus.

B. The profuse growth of the meningococcus in Loeffler's serum and the absence of any growth of the gonococcus on this medium. Some claim to have seen a slight growth of the gonococcus.

C. We never obtained growths of the gonococcus in agar. At times the meningococcus grows on agar. Some writers have noted slight growths of the gonococcus on agar. In any event a good growth on agar speaks against the gonococcus.

In serum bouillon media and serum glucose bouillon media the two organisms grow practically in the same way. I have repeatedly noted that the growth of the gonococcus in fluid media, if the observations are carefully made, is on top of the fluid in the form of a white scum. This feature of the gonococcus has as far as I have been able to determine never before been described. I hope to go into this subject in a later paper dealing with the biology of the gonococcus.

7. None of the three organisms under discussion causes precipitation in any of my serum sugar media. According to our experience staphylococci always precipitate in two per cent glucose serum agar. By the use of this medium the occurrence of the confusion of staphylococci with meningococci, which Ghon and Albrecht suspected in some of the reported observations, can be avoided.

8. As to the frequency of finding the meningococcus in cases of cerebro spinal meningitis — we have studied thirty cultures in twenty cases—in some, repeated examinations were made. In all the cases we found the diplococci in spreads or in cultures. In the first seven cases we failed to obtain the organism culturally in one.

In the last seventeen cases we always succeeded in obtaining cultural results. These seventeen cases were studied by the aid of the serum glucose media. At times the organisms are found in spreads at first and not later. Cultures may be positive first and negative later. We believe the diagnosis can always be established if the examinations are made early. In cases of long standing, cultures and spreads might be found negative.

Ghon reports twenty-two positive results in thirty cases, (but some fluids were sent from a distance). Osler found the cocci in spreads or in culture, twenty-seven times in thirty cases. Councilman, Mallory and Wright examined puncture fluids in fifty-five cases. The diplococcus was found in spreads or in cultures in thirty-eight. Gradwohl, (St. Louis), describes cultures which can hardly be considered as being those of the meningococcus.

9. We obtained results with small amounts of fluid when we used the two per cent serum glucose agar. We usually poured one-half to one cubic centimetre of fluid into a tube of the medium. Twice a day the condensation fluid and added fluid were allowed to flow over the surface of the medium (Heubner's method). It often required forty-eight hours for a result. Once it required seventy-two hours.

The occurrence of a growth of a Gram-negative diplococcus which shows no or but slight growth on agar, no growth on gelatin nor on potato nor on bouillon in twenty-four hours, which causes no change in litmus milk in the same time, and which grows profusely on Loeffler's medium, is sufficient to make the presence of the meningococcus a certainty.

These final remarks hold true provided media of certain titres are used. From our experiences we would say that the media not containing serum should be neutral or slightly alkaline to phenolphthalein. The serum media should be made from agar which is one-half or one per cent acid. The subject of titer is of extreme interest with regard to the meningococcus and gonococcus. We hope to report further on this aspect of the subject.

Discussion.

Dr. Brooks: Several years ago I studied a series of cases of purulent meningitis. This was before Dr. Libman's culture media had been devised. I became so mixed up with the various forms of meningococci that I did not dare to publish the results. I have found it very difficult at times to differentiate between the meningococci and the micrococcus catarrhalis. I also found that animal experiments were very uncertain. I also found that large quantities of culture were usually required in order to obtain growth of the meningococcus. I believe that the work of Dr. Libman and Dr. Celler is most important and will be particularly appreciated by those who have done any work with these organisms.

EXPERIMENTS RELATING TO THE FIXATION OF STRYCHNINE BY ANIMAL TISSUES.

G. LANGMANN, M.D., AND S. J. MELTZER, M.D.

While it was formerly supposed that strychnine, whether taken by the mouth or injected hypodermically, combined with the tissue, Dragendorff and other observers proved that it left the system unaltered and was principally excreted by the kidneys within less than forty-eight hours. Von Czyhlarz and Donath revived this question in 1900 by claiming that strychnine when injected into a ligated extremity of a guinea-pig was neutralized by contact with the living tissues. Repeating the same experiments, we were unable to confirm these statements; we believe it probable that absorption is impaired by the constriction and that sufficient elimination takes places so that at no time an efficient minimum was reached. Carrara, however, sustained the theory of v. Czyhlarz and Donath by apparently conclusive experiments. After checking all elimination through double nephrectomy he found that strychnine injected into a ligated extremity caused no symptoms. Although this premise sounded very plausible it was never tested by experiment. Meltzer and Salvant found that rabbits, at least after double nephrectomy would tolerate the gradual injection of the triple lethal dose without exhibiting the least effect of strychnine. The same experiments were repeated by us on guinea-pigs and it was found again that after double nephrectomy doses far above the lethal may be injected without obtaining a single symptom of strychnine poisoning provided that not too large single doses were used and that they did not follow each other too closely. The gradual injection of as much as twenty mgr. per kilo did not even cause a hyperaesthesia although the lethal dose for normal animals is four mgr. per kilo.

These experiments, therefore, cannot be adduced to sustain von Czyhlarz and Donath's theory. It was furthermore established that strychnine was ineffective provided it was not injected within the first three hours after nephrectomy. Previous to that period even subminimal doses proved fatal. Some of the nephrectomized animals exhibited a ***subtetanic reaction***, a peculiar continuous vibration, ending in death within an hour. It seems likely that during the hours following nephrectomy the system elaborated a compensatory mechanism of elimination for the injection of strychnine into a ligated extremity proved to be fatal if nephrectomy was performed and the ligature loosened three hours after the injection.

Discussion.

DR. LEVENE: I have made the same observations that Dr. Langmann has made in support of his theory as to the reaction of the organisms on strychnine. A paper has appeared during the year on the antitoxic effect of nerve tissue on tetanus toxin. It is claimed by the author that nerve tissue has not the power to absolutely neutralize tetanus toxin but to a certain extent diminishes its effect. Tetanus toxin was given to an aminal mixed with the pulp of brain tissue. It was found that smaller amounts of antitoxin were needed to save the life of the animal that when the toxin was injected directly without the brain emulsion. This author therefore claimed a specific antitoxic effect for the brain emulsion. It seems to me that the simpler explanation would be that the tetanus toxin acted more slowly in colloidal solution than when injected directly and that therefore less antitoxin was necessary to save the life of the animal.

DR. MELTZER: I do not arise again to defend my own experiments but those of another. Wasserman's experiments were not performed by mixing brain tissue and tetanus toxin but the toxin was injected into one side of the animal and the brain tissue into the other side.

Dr. Levene: I did not have reference to Wasserman's experiments.

REMARKS ON VASO-MOTOR NERVES, WITH DEMONSTRATIONS.

S. J. MELTZER, M.D., AND CLARA MELTZER, M.D.

Since 1852 the sympathetic has been considered the sole or main vaso-motor nerve of the ear. This is the impression one gets from examining text-books on physiology. We investigated the subject in a series of twenty-one rabbits. Without entering upon a description of the operation the following results may be given: In about one-half of the animals the dilatation of the vessels of the entire ear after section of the third cervical was well marked and as good, if not better than that following section of the sympathetic. In only two, section of the cervical had almost no effect. In the balance the dilatation was chiefly in the vessels of the upper part and sides of the ear. Section of the left cervical gave more distinct effects than that of the right. It seemed that this applied also to the sympathetic. In a number of animals we especially noted that white the effect of the section of the sympathetic is considerably diminished in three or four days, that of the cervical continues in most animals undiminished for a much longer period. We got the impression that the color of the animal had some influence. Stimulation of the peripheral cut end of the cervical also gave in many cases a greater constriction than the stimulation of the sympathetic. In some animals the constriction affected the vessels of the entire ear; in others it affected only the vessels of the top and sides; and in a few there was no effect. In all cases both sides were different, the left side usually giving greater effects. A few cases were observed in which stimulation of the cervical had very little or no effect; nevertheless section of this nerve caused considerable congestion of the ear which shows that the cervical maintained a vaso-constricting tonus. This means that normal stimuli are more adequate than the artificial ones which we usually employ in experiments. These experiments demonstrate that the blood vessels of the rabbit's ear are under the control of two separate sets of nerves, the cervical and the sympathetic, which can substitute one another—a striking example of collateral innervation.

Discussion.

DR. LEVENE: I have been interested in Dr. Meltzer's statement that the color of the animals seemed to have some influence on the results of the experiments. In the work which I have done requiring intravenous injections I always preferred white rabbits. I should like to know whether Dr. Meltzer also found that the vessels of the white rabbit were more developed and whether that explained why the widening after the cutting of the nerve was greater? Was there not a difference between the results of the operation in the right side and on the left side? In nature these arteries are larger on the right side than on the left. Would not the difference in the normal caliber of the arteries on the two sides interfere with the measurements after cutting of the cervical nerves?

DR. S. J. MELTZER: In regard to the question of the different results according to the color of the rabbit I would not wish to go on record. Hundreds of rabbits would have to be studied before a conclusion in this regard could be positively demonstrated. With regard to Dr.

Levene's second question I may say that the differences between the right and left sides in the widening of the vessels after section of the nerves is not a matter of theory but of observation. We have seen the blood vessels before the section of the nerves and knew that there was no such preformed anatomical differences between the two ears. Nor would this have anything to do with the question of stimualation. By stimulating the nerves on the left side a greater effect is produced than by stimulating those on the right side. This fact has nothing to do with the original size of the vessels.

GLIOMA OF THE BRAIN.

T. C. JANEWAY, M.D.

I do not present this specimen because of its remarkable rarity but because the case had a very characteristic history and ran an unusually rapid course. The specimen was obtained from a man of forty who entered St. Vincent's Hospital on the twenty-fifth of October. He gave the following history: He had been a moderate drinker and had chancroids; beyond this there was nothing of any particular importance in his past history. On Labor Day his first symptoms of brain trouble appeared in the form of an attack of dizziness while in a parade. He was compelled to rest and to return home. The same day he travelled to Newburg and while there he fainted and had a repetition of the vertigo. From that time the attacks of vertigo succeeded each other, coming several times a day, and he began to stagger and to run into objects. He had severe headaches which were very much intensified by any movement. The pain at first was all over the head, but in the latter part of his illness was confined to the right side. He had attacks of vomiting which he referred to taking milk. He was sent to the hospital with a diagnosis of brain fever. On admission he had staggering and exaggerated reflexes, both of the patella and of the arm. The temperature was normal. The right pupil was dilated. Dr. Callan reported optic neuritis which was more pronounced in the right eye. He had perfect control over his bladder and rectum. From that time until December 6, when he died, he was put upon mixed treatment. He was seen by the different attending physicians and by Dr. Starr, and the clinical diagnosis was made of gumma of cerebellum. He improved for a time, but the improvement soon ceased and he became delirious, vomited freely, had intense deadache, and died rather suddenly. At autopsy the following condition was found: He had a fairly marked flattening of the convolutions all over both hemispheres. There was a marked flow of fluid on opening the lateral ventricles. Section of the cortex showed nothing particularly abnormal. On opening the cerebellum in the median line one came upon a small irregular cyst filled with yellowish contents, surrounding which was a narrow area of tissue which was hardly demarcated from the normal white matter of the cerebellum in which it lay except that it seemed to be a little firmer than the rest of the tissue. The lower part involved the right superior peduncle. This portion was in color very much like the normal tissue; there was no distinct line of demarcation. The ragged cyst in the center was filled with yellow contents which showed broken down granular detritus. Sections from the edge showed perfectly typical glioma with very numerous thin-walled blood vessels. Sections from the peduncle showed very cellular glioma with occasional ganglion cells scattered throughout, which were apparently inclusions in the tissue. A point of interest was whether the initial symptom was due to hemorrhage into the solid portion of the tumor and whether the glioma had been of more than two months' duration.

Discussion.

DR. BROOKS: It seems to me rather remarkable from the location of the tumor that it could have existed long before the onset of the first symptoms. I believe that glioma of the brain often develops very rapidly. In my experience glioma of the cerebellum is much rarer than glioma of the cerebrum.

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Dr. James Ewing, *President.*

A CASE OF BOTHRIOCEPHALUS, WITH REMARKS ON THE OCCURRENCE OF BOTHRIOCEPHALUS IN AMERICA.

W. N. BERKELEY, M.D.

Dr. Berkeley presented specimens from a case of Bothriocephalus. The patient was a native of Russia, forty-six years of age, a female, married, and had several children. She came to this country a few years ago. She had been passing segments of the worm for eight years, but had never had medical advice. She was in good health, had no anemia, and complained only of vague digestive complaints. Treatment was begun and two days later she brought the worm with the head complete to the dispensary. Dr. Berkeley said that he had been able to find no references in the literature to any cases endemic in the United States. Ritchie in his recent article on Parasites *(Encyclopedia Medica)* said that the worm was "seldom seen in England", but made no mention of cases in this country. Dock had observed three cases in this country, one in Colorado and two in Texas, both of which he was satisfied were imported. Osler also noted that there were no endemic cases. In the last edition of *Braun's Thierische Parasiten* the name had been restored to its older form, Dibothriocephalus. Braun could mention only a single case from the United States, not stating whether this was believed to be endemic or imported. Dr. Berkeley had observed three other cases in the last four years, all in the same class of Russian immigrants. In these cases there were no signs of anemia and the patients complained only of indefinite digestive disorders. The parents of one patient, a small girl, claimed that she had never passed segments of the worm until three months before consulting the doctor, and years after her arrival in this country. On examination it was decided, however, that this was probably not correct, and the case was classified as an imported one.

Discussion.

DR. THEODORE C. JANEWAY said that he had seen a case of Bothriocephalus during the week in a woman from Finland. She was in good health; hemoglobin was eighty per cent. Her symptoms were similar to those of Dr. Berkeley's case. She had noticed passing the first segments of the worm eight years before, but said she had not seen them again until recently. The worm obtained was twenty-four feet in length.

Dr. James Ewing said that some years ago he had presented to the Society three large specimens all taken from the same subject, a Swede, who claimed not to have eaten raw fish for seventeen years. He had been entirely well and had had no signs of anemia.

DEMONSTRATION OF THE HEMOSIDERIN REACTION IN CORNEAL VACCINE BODIES.

JAMES EWING, M.D.

Dr. Ewing said that about six months before he had had occasion to bring together some evidence regarding the nature of vaccine bodies. This evidence pointed to the view that red blood cells sometimes assumed the position and exhibited the staining qualities of vaccine bodies. He had not claimed that all vaccine bodies were of this nature, nor did he wish to go so far yet. He merely wished to present some evidence which he had obtained in favor of this theory. The hemosiderin reaction he had not been able to get in every instance; in fact, in the majority of cases the stain had been a failure, and in some sections he had succeeded in getting the blue stain in only a portion of the vaccine bodies. The specimens were hardened in bichloride saturated in .6% salt solution, cut in paraffin and allowed to remain twenty-four hours in potassium ferrocyanide, and six hours in hydrochloric acid. The blue color was seen only in the center of the vaccine body and by staining with eosin or safranin the outer portion of the body took on a red stain. In many sections of human tissues the vaccine bodies gave only a faint diffuse reaction. The meaning of the blue stain thus obtained in the center of the vaccine bodies he was unprepared to discuss. He thought some would regard it as evidence that these bodies contained free iron and were derivatives of red cells. Of course, the fact that the stain was not obtained in every instance was a suspicious circumstance.

LIMITS OF A SPECIFIC REACTION IN THE SERUM TEST FOR BLOOD.

JAMES EWING, M.D., AND ISRAEL STRAUSS, M.D.

Dr. Ewing presented tables showing the results of experiments, conducted with Dr. Israel Strauss, relating to the limits of a specific reaction in the serum test for blood; that is, the test by which it was believed to be possible to distinguish between all varieties of blood. He said it was already known that reactions among so-called specific anti-sera were only quantitative and not strictly specific. The specific anti-body developed in the serum of the rabbit treated with human blood would produce a reaction in a variety of other bloods as well as in human blood, Only at a certain point of dilution did the heterologous bloods drop out, leaving the reaction only in the human blood. It was therefore very necessary to determine the solutions of blood with which one worked in order to estimate results correctly. One series of experiments were made on the effects of the serum of a rabbit, which had received multiple injections of beef blood, on various other bloods. The bloods tested were human, goat, cat, chicken, sheep, horse and beef. Various dilutions were used, from 1–10 to 1–1500. When the serum was added to all these different bloods in a dilution of one part of serum to five parts of blood, practically the same results were obtained in all. At the end of thirty minutes there was a flocculent precipitate in human blood; the reactions in beef and goat blood were more distinct than in the other, and it was not possible to distinguish the beef blood. In a dilution of serum of one to ten, human blood gave little reaction; chicken, horse and rabbit bloods gave no reaction at all. The beef and goat were about the same. At one to fifteen, human blood dropped out entirely. The sheep still reacted. In the lower dilutions it had been about the same as the goat. Comparison of the beef and goat at one to fifteen showed rather in favor of the goat. At one to twenty, sheep blood still gave a distinct reaction, being turbid at the end of three hours. The beef gave a flocculent precipitate. At one to thirty, the sheep blood dropped out; beef and goat blood each gave a prominent turbidity, about equally strong. At one to fifty, the beef blood reacted as strongly as ever, but the goat blood had dropped out almost entirely. This showed that the reaction was specific only in high dilutions. In order to get a specific reaction with the beef-rabbit serum, it was necessary to dilute the serum up to one to fifty. The dilution of the serum added seemed to be more important than the dilution of the blood to be tested. Experiments were then made with humanized rabbit serum. Two sera were tested, one prepared by Dr. Strauss, and one by Dr. Paine. With Dr. Strauss' serum tests were first made at a dilution of one to five. There was no reaction with dog, cat or horse serum. There was a slight reaction in sheep, beef and goat bloods. The reaction in human blood, however, was not sufficiently distinct.

At one to ten goat blood dropped out. The sheep blood still reacted, but in diminished intensity. Human blood was the same. The beef reaction was slightly diminished. At one to twenty, there was nothing left but the very prominent reaction in human blood. This seemed to be encouraging for the specificity of the test for human blood until the other serum was tested, when different results were found. With this serum at one to five, the sheep, beef and human bloods showed good reactions. There was nothing with dog, cat or horse. This serum was evidently stronger than the first. At one to ten, human, sheep, beef, and goat blood still showed about the same reaction. At one to twenty, the reaction in the human blood was much the most distinct, but the reaction in sheep and beef blood was still quite as distinct as some obtained in human blood with the other serum. These results showed that the dilutions of this particular serum must be made above one to twenty before one could eliminate all but human blood. Some of Dr. Ewing's conclusions were; that it was unsafe to give credence to anything except a flocculent precipitate, that the time in which this flocculent precipitate occured was of the greatest importance. Before two hours it never occurred in his experiments in any blood except that against which the serum was prepared, if the test serum had been diluted at least one to twenty. It would seem that reliable results could not be assured unless the test serum was diluted at least one to fifty.

Discussion.

Dr. W. H. Park asked whether Dr. Ewing knew what the rabbit serum would have done before the injections of human blood. He considered that it was very important to know the agglutinating properties of the blood before treatment, so as to judge how much of the agglutination was due to the normal blood, and how much to the influence of the human or other blood injections.

DR. EWING said that he realized the importance of Dr. Park's statements. This work had only been done as a beginning. At the time he had himself thought it very important to know what the animal's blood would do before the experiments were made. In the first case, weak dilutions were practically inert in all the bloods tested.

DR. F. C. WOOD asked Dr. Ewing whether the strength of the dilutions of the blood to be tested were determined with accuracy or whether they were merely roughly determined.

DR. EWING said that the dilutions of blood had been determined with great accuracy, as was shown by the tables. A more important point, however, was the strength of the serum.

DR. OTTO H. SCHULTZE asked whether in tests made with humanized rabbit serum there had not been some differences which the tables shown had not brought out. Dr. Ewing had said that in the various dilutions all the reactions were practically the same. Had there not been some difference in the amount of the precipitate dependent upon the strength of the dilution used?

DR. EWING said that the stronger the dilutions of the blood the larger in most instances were the amounts of precipitates obtained.

DR. S. J. MELTZER asked whether Dr. Ewing had followed out these tests with regard to the character of the food of the animals he experimented with. It would appear that his animals could be classified into two groups; carnivorous and herbivorous animals. It appeared to him quite plausible to assume that the proteids of the bloods of animals of the same group had among themselves a greater similarity than that between the animals of different groups. It would therefore be not unreasonable to expect to find that the precipitin reactions were less specific with the blood of animals which were fed in the same manner than with the blood of animals which were fed differently.

DR. EWING said that he had not yet got to this point. Nuttall he knew, had attempted to classify animals by the serum reactions. He himself did not believe that the subject was in such a position that it was possible to draw reliable conclusions of this character. Investigators were in no position to eliminate just now all the disturbing results of the peculiarities of the particular animals with which they worked. He had, with the other sera, tested the serum of a chicken immunized against rabbit blood, which acted so peculiarly that he had thought it best not to tabulate the results.

A STUDY OF A BACILLUS RESEMBLING THE BACILLUS OF SHIGA, FROM A CASE OF FATAL DIARRHŒA IN A CHILD; WITH REMARKS ON THE RECOGNITION OF DYSENTERY, TYPHOID, AND ALLIED BACILLI.

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Several reasons have led us to report the results of our study of the organism isolated from this case of fatal diarrhœa. Chief among these is the vital importance of establishing beyond doubt the etiology of the various forms of diarrhœas and dysenteries. Upon such establishment of etiology must ultimately depend the rationale of hygienic, diagnostic, and therapeutic measures —especially those of serum therapy, and diagnosis by serum reactions—upon which the recognition and cure of the disease or protection from the infective agent must be based. Moreover, there is the greatest need, in the present state of our knowledge of the etiology of dysentery, of the most careful study, description, and especially comparison of the bacterial forms supposed, in different cases and various localities, to be of etiological significance in the same or various forms of this disease.

As will be brought out more fully in detailing the peculiarities of the organism we are about to describe, the organisms isolated from cases of dysentery—apart from a determination of superficial resemblance in growth characters on the usual nutrient media and their reactions in the presence of the more commonly employed sugars, —dextrose, lactose, and saccharose—have been largely identified by their supposed specific agglutination reactions in the presence of serum from dysentery patients and immune animals. That there are serious objections to placing too complete confidence in such measures alone, we believe will appear from our study.

The bacillus of acute dysentery, or diphtheritic colitis first described by Shiga (1) in 1898 as etiologically connected with the disease in Japan, and the bacillus isolated by Kruse (2) in 1900, from the same disease in Germany, have finally after much comparison and discussion of minute differences been recognized as identical species. Under the stimulus of Flexner's (3) work, the same species has undoubtedly been isolated from cases occurring in America, as is shown by the corresponding cultural characters and serum reactions of the organism isolated in New Haven, Conn., and known as culture "New Haven" (4). Flexner's culture isolated by him in 1899 while in the Philippines is not admitted by all observers to be identical with the preceding, although Kruse—aside from the general weaker growth of the Flexner bacillus, and minor differences in its agglutinating reactions, which are as a rule less marked in serum from dysentery cases than the reactions of "Shiga," "Kruse," and the "New Haven" cultures—could determine no specific differences, and concluded that the variation was not greater than that occurring among various true typhoid cultures. Shiga (5) in his latest article is practically of the same opinion, and claims to have gotten similar reactions to those given by Flexner's bacillus with cultures of his own, when these were grown for several generations in milk. From this he believes the Flexner bacillus to be simply a slightly modified form of the true Bacillus dysenteriæ.

Martini and Lentz (6), however, and particularly Lentz (7) in a separate article on the cultural differentiation of these organisms, claim to have found not only discrepancies in agglutination, but cultural differences of fixed value in the Flexner bacillus, as brought out in mannit-litmus agar (Drigalski's medium). To a discussion of this point we shall return later.

The bacillus, to a consideration of which we invite your attention, was isolated from the contents of a section of the colon of a child dead of an acute diarrhœa. We are indebted to Dr. David Bovaird for the material, and as he is here this evening we leave it to him to tell you something of the clinical course of the disease, and of the pathological changes found at death.

Method of Isolating the Organism.—The method employed by us for isolating the organism was as follows: The contents and scrapings from the mucosa of the gut were diluted in broth and platings were made from this emulsion by transferring one to several loopfuls to the medium* recommended by one of us (Hiss) (8) for isolating the bacillus of typhoid fever. In this medium the colonies of the bacillus of Shiga do not form threads, as do the typhoid bacilli, and may usually be distinguished from the colonies of colon bacilli and allied forms, by being smaller and lighter in color. Transplants were made from the small, light colored, transparent colonies which were present, into tubes of the semisolid medium described by Hiss (9) in 1897. By the use of this medium, which appears to us much superior to the glucose agar recommended by other workers, organisms corresponding in character to the Shiga bacillus may be readily recognized. In this semi-solid medium when inoculated at 37° C., the bacillus of Shiga, possessing no active motility, does not spread out in the medium and cloud it; but its growth is confined to the original line of inoculation. Neither does the dysentery bacillus form gas in the medium, from the one per cent of glucose which is present. All colon bacilli form gas in the medium and are also distinguished by other characters, more or less marked, which depend upon their degree of motility. Typhoid bacilli are readily differentiated by clouding the medium uniformly,

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* Composed of agar, 15 gm.; gelatin, 15 gm.; Liebig's meat extract, 5 gm.; sodium chloride, 5 gm.; and dextrose, 10 gm. No acid or alkali is added. See reference No. 8, p. 156.

If some such semi-solid medium as this had been employed, instead of dependence being placed on the microscopic test alone, much of the uncertainty and consequent discussion regarding the motility or non-motility of the bacilli described by Shiga and Flexner, it seems to us, might have been avoided.

As pointed out by Hiss some time ago, the character of the growth of the bacillus of Shiga in this semi-solid medium in tubes and its inability to form threads in the typhoid plating medium, were among the exceedingly few cultural characters until recently known by which this organism could be separated from the bacillus of typhoid fever.*

Description of the Bacillus.—An organism answering to the characters shown in the semi-solid medium by the Shiga bacillus was found to be present in the gut contents of our case, and was subjected to various tests to determine if possible its further identity with various cultures of Shiga's bacillus. Three cultures of this organism sent to us by Prof. Flexner have been studied. These, as has been stated, are the cultures known as "Kruse," "Flexner," and "New Haven." "Kruse" is the culture isolated during an epidemic in Germany. "Flexner" is one of the cultures obtained by Prof. Flexner while in the Philippines, and "New Haven" sometimes referred to as "Seward," was from a case of dysentery occurring at New Haven, Conn.

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* See reference No. 8, p. 165.

Morphology.—The organism is a short, fairly stout bacillus, with rounded ends, in some cultures almost coccoid in form. It occurs singly, but often in pairs, and rarely short threads may be seen. There is a tendency in some preparations to occur in clumps. The bacillus stains with the anilin dyes, but as is the case with Shiga's bacillus, the staining of all the bacilli in a preparation is not equally intense. Near well stained individuals it is the rule to find many which have taken the dye very poorly. The staining of the protoplasm of individual bacilli is also at times irregular. The organism is decolorized by Gram's method. Spore formation has not been observed. The bacillus is not motile. Flagella stainings have not, so far, been made. No capsules have been noted.

In general morphology and staining reactions the organism answers most closely to that of the dysentery bacilli as represented by Kruse's culture. Flexner's bacillus is not so stout and is longer than ours, thus corresponding morphologically more closely to the bacillus of typhoid fever.

Cultural Characters.—The bacillus grows well on the the culture media, and corresponds on these in all essential respects to the Shiga bacillus. Gelatin is not fluidified; nor is indol, according to our tests, produced. On the usual nutrient broth, which is clouded uniformly by the growth, a small pellicle may be formed after ten or twelve days at 37° C. When a fermentable sugar is present in the broth no pellicle is formed. The same observation holds good for typhoid and colon bacilli. This absence of pellicle is probably accounted for by the ease of obtaining oxygen from the sugar and subsequent inhibition of growth by acid production. A failure to recognize this fact has undoubtedly led to discrepancies in decriptions of organisms. Some facultative organisms, usually not forming pellicles will do so in sugar free media, or at all events grow more abundantly in the upper portions where the necessary oxygen is present. None of our cultures of true Bacillus dysenteriæ have, however, formed pellicles.

Fermentation Tests.—A study of the organism in dextrose, lactose and saccharose bouillon in fermentation tubes shows a complete correspondence with the bacillus of Shiga, as represented by the cultures "Kruse," "New Haven," and "Flexner." All of these organisms ferment dextrose with the formation of acid and a clouding of the open and closed branch of the fermentation tube. Neither lactose nor saccharose are fermented by any of those organisms, hence are not available for anaerobic growth and the closed branch of the tube remains clear. These bacilli are not able to grow anærobically in broth not containing some available carbohydrate or allied source of oxygen supply.

It has been the common practice in our laboratory for several years past to test organisms, especially those of the typhoid, Gärtner, and colon groups, on one per cent. mannit broth in fermentation tubes. A test of organisms in this medium has in our hands always served to differentiate cultures of Shiga's bacillus—"Kruse," "New Haven," and Flexner"—from typhoid bacilli. This point was first noted about two years ago in our laboratory by Dr. Charles Norris, who in observing the fermentative activities of certain members of the typhoid and Gärtner groups, tested the cultures "Kruse" and "Flexner" sent to us by Dr. Flexner shortly after his return from the Philippines. Typhoid bacilli, Norris found, utilized mannit with acid production and clouded the closed branch of the fermentation tube, while the dysentery cultures could not ferment mannit, and did not grow in and cloud the closed branch of the tube, which in glucose free broth always remained clear. This fact was called to the attention of Prof. Flexner at that time. The organism isolated by us when grown thus in mannit does not correspond in its action to the cultures "Kruse," "New Haven" and "Flexner" but ferments mannit and clouds the closed branch of the tube as do the typhoid bacilli. In bouillon made from maltose of high purity it can, however, be differentiated from typhoid cultures. Typhoid cultures ferment maltose with acid production and cloud the closed branch of the fermentation tube, while our organism does not ferment maltose nor cloud the closed branch.

It is well to note that cultures of Petruchsky's Bacillus fecalis alkaligenes can be distinguished from dysentery, typhoid and allied bacilli, by its inability to ferment any known carbohydrate (at least, anærobically) or to cloud the closed branch of the fermentation tube.

Serum-Water Media.–A most striking differentiation of organisms belonging to the dysentery, typhoid, Gärtner and colon groups is afforded by a study of these organisms in serum-water media. This medium as a basis for studying fermentative activities was devised by one of us (Hiss) for use in the differentiation of pneumococci from streptococci.

The medium is composed of clear beef serum, one part, and distilled water, two parts.* This mixture can be boiled without causing a coagulation of the albuminous bodies present. The medium after boiling is an opalescent fluid. As was pointed out in the original communication on this subject, this medium is practically, if not absolutely, sugar free. The original monosaccharid content of the blood is rapidly destroyed after drawing, by the action of the so-called glycolytic ferment of the blood. That this is still active in serum may be demonstrated by adding small amounts of dextrose to sterile serum, and then allowing this to digest at 37° C., for an hour or so. Subsequent fermentation tests with organisms will show that the sugar has entirely or partially disappeared, according to the amount added, as determined by acid or gas production. In using the medium as a basis for fermentation tests it is necessary to boil it before adding the sugars, as many of these are acted upon by the enzymes of the blood,—diastase, maltase (glucase), etc.— This may also be easily demonstrated by digesting the sugar, especially dextrin and maltose, for a short while in the unheated serum water mixture, maltose being rapidly destroyed and split into dextrose, and dextrin quickly changed to maltose and then to dextrose. The medium is therefore made by first heating the serum-water at 100° C. for a short time, and then adding usually one per cent of sugar desired. To this is added litmus solution (Merck's highly pure litmus, 5% solution in water) in the proportion of one per cent. The medium is then tubed and may be sterilized at 100° C. for ten minutes on three consecutive days without fear of changes taking place in the sugar from the application of the heat.

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* Beef serum, one part, distilled water, three parts, is better as it is less opalescent.

The sugars so far tested by us are dextrose, galactose, mannit, maltose, lactose, saccharose, and dextrin. These sugars serve eminently well to differentiate our organism from the dysentery bacillus of Shiga, and also to distinguish between these and organisms of closely allied characters, such as typhoid bacilli, B. fecalis alkaligenes, colon, and the organisms of the Gärtner group. This is shown by the following tests of organisms:

B. fecalis alkaligenes: None of the sugars are fermented; all of the media remain blue and unchanged.

B. Shigae: *Dextrose* and *galactose* are fermented with acid formation as shown by a reddening and solid coagulation of the medium. Mannit, maltose, lactose, saccharose and dextrin are not fermented, the media remaining blue and fluid. This is true of "Kruse," "New Haven" and "Flexner."

Bacillus Y (Hiss and Russel): *Dextrose*, *galactose* and *mannit*, are fermented with acid production, as shown by reddening and coagulation of the media. The fermentation of mannit differentiates this organism from B. Shigae, as represented by the cultures "Kruse," "New Haven" and "Flexner." The maltose, lactose, saccharose and dextrin tubes remain fluid and blue.

Bacillus "48": From stool of typhoid fever patient in 1897. Same reaction as above with the exception that the mannit medium is not coagulated throughout the entire depth, but shows a blue fluid layer at the top. This organism, however, is actively motile and thus further distinguished from "Y."

Bacillus Typhosus: *Dextrose*, *galactose*, *mannit*, and *maltose* and *dextrin* are fermented with acid production, as shown by a reddening and solidification of the media. *Dextrin* tubes first show a change to purple, and later coagulate in the lower portion leaving for some time a blue fluid layer above. Lactose and saccharose media remain unchanged and blue. The fermentation of maltose and of the dextrin medium serve to differentiate typhoid cultures from our organism and from the culture "48."

Bacillus "48" deserves further mention. It was isolated by Hiss in 1897 from the feces of a New York Hospital patient supposed to be suffering from typhoid fever, and was thought at first to be a true typhoid bacillus; but was subsequently looked upon as doubtful as it did not form thready colonies in the typhoid plating medium and, although clouding the tube medium uniformly without gas production, formed a thin pellicle at the surface of the medium. This is never the case with true typhoid cultures. It had been preserved in sealed tubes until a short time ago when it was re-examined and found to differ from typhoid bacilli in its action on maltose and dextrin. Although its sugar reactions correspond very closely to those of our bacillus "Y," it is as above noted to be readily distinguished from it by its motility.

Agglutinating Reactions.[1]—Unfortunately we were not able to obtain a specimen of blood or serum from the patient from whose intestine our bacillus was isolated, so that a most important link in the chain of etiological evidence is lacking. A study of the agglutinating reactions of the bacillus have, however, been made with various normal and immune sera, and with the serum of an animal immunized with the bacillus itself. The following interesting and, it seems to us, very important results have been obtained.

Normal Human Blood:—The results of tests against supposedly normal human sera were as follows:

Serum A. Adult man, in good health; no history of bad diarrhœic or dysenteric attack. This serum did not agglutinate the bacillus in any dilution.

Serum B. Placental blood. No history furnished. Positive reaction 1–20, two hours. 1–30, two hours was negative.

Serum C. Adult man in good health. Two years ago while in Porto Rico suffered from a prolonged attack of diarrhœa, which was not, however, considered dysenteric in character. Positive reaction, 1–80, in two hours. Negative, 1–100, in four hours. This serum on account of the previous diarrhœa probably should be excluded from the normal list.

Human Sera, Dysentery:

Serum A. From a soldier with chronic dysentery. Acute attack in the Philippines two years ago. Another attack subsequently in Porto Rico. Positive reaction with our bacillus, 1–20, one hour. "Flexner" did not react at 1–20. "Kruse," --1–10, —1–40; "New Haven," ±1–10; ±1–20; —1–40.*

Serum B. From a soldier with chronic dysentery. Sent to us from the military hospital in Washington. Acute attack of dysentery in the Philippines two years ago. Our organism reacted 1–40, one-half hour. "Flexner" gave no reaction. "Kruse" was positive 1–20; minus, 1–40, one and one-half hour. "New Haven" positive 1–20; negative, 1–40, one and one-half hour.

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* Indicates a partial reaction.

Normal Horse Serum:

Bacillus "Y"	+1–40, one-half hour:	±1–80.
"Kruse"	+1–20;	±1–40.

Dysentery Horse Serum: From a horse immunized against culture "New Haven." Sent to us by Prof. Flexner.

Bacillus "Y"	+1–400;	±1–500,	twenty hours.
"New Haven"	+1–100;	±1–200,	twenty hours.
"Flexner"	+1–40;	—1–200,	twenty hours.
Bacillus "48"	—1–1;	—1–50,	twenty hours.
B. typhosus	+1–20.		

Normal Rabbit Serum:

Bacillus "Y" ±1–2; —1–10, 1–20, 1–100, two hours.

Typhoid Rabbit Serum: Highly immunized against typhoid. Exact titre against typhoid originally 1–20,000.

Bacillus "Y"	+1–500; +1–4,000.
"New Haven"	—1–20.
Bacillus "48"	—1–25 and 1–100, twenty hours.

"*Y*" *Rabbit Serum:* This animal received several inoculations of boiled cultures of "Y". The serum agglutinated "Y" in dilutions as high as 1–500. "Kruse," "New Haven" and "Flexner" did not react in any dilution (—1–10; —1–500). Bacillus "48" also showed no agglutination. B. typhosus reacted at 1–80; ±1–100 in twenty hours.

Normal Beef Serum:

Bacillus "Y"	+1–200;	+1–320, four hours.
"Flexner"	+1–10,	—1–20.
"New Haven"	+1–10;	—1–20.
"Kruse"	+1–10;	—1–20.
B. typhosus	+1–40;	+1–80, twenty hours.

The results of these serum tests are important and indicate to us, after a careful search of the literature of dysentery, that we are in all probability dealing with an organism not hitherto described. It is readily seen from our tests that "Y" agglutinates with dysentery serum from human infections and from immunized animals in most instances quite as well as, and in some better than do bacilli fully identified in all respects with the bacillus of Shiga. The various dysentery-like baccilli described by other observers, although showing some agglutination in the presence of dysentery sera, have been agglutinated to a markedly less degree than true dysentery bacilli, and for this reason alone have in several instances been excluded from recognition as fully identical with Shiga's bacillus. This is true of the organism described by Kruse as the bacillus of pseudodysentery of the insane. The organisms placed in this class were, according to him, so far as he could determine, in all respects similar to his and Shiga's dysentery bacillus in cultural characters. They were differentiated by not agglutinating with true dysentery serum, but with the serum from insane patients. The true bacillus of Shiga on the other hand did not agglutinate with these sera in the same dilutions. These pseudodysentery cultures were agglutinated in normal sera in 1–50, which is higher than that usually shown by the true dysentery bacillus. Kruse has found that his true dysentery organism agglutinates in normal sera as high as 1–20, and exceptionally 1–50. In his later paper, however, he thinks this may have been due to previous infection.

Another point of interest is the high agglutination of our bacillus with sera from animals immunized against typhoid. Here "Y" shows a very close relationship to the bacillus of typhoid. This bond is strengthened by the fact that typhoid cultures also show fair agglutination in "Y" immune serum. Both Shiga's bacillus and typhoid call forth agglutinins which have an affinity for the receptors of our bacillus "Y". "Y" immune serum on the other hand contains some agglutinins active for typhoid bacilli but none, so far as our experiments go, which affect Shiga's bacillus.

"Y" and typhoid bacilli, therefore, call forth some agglutinins in common or have receptors capable of anchoring certain agglutinins of each. "Y" it may be, anchors all of the agglutinins called forth by Shiga's bacillus and probably other agglutinins normally present in the serum tested. This is indicated by its higher agglutination in the dysentery horse serum than that shown by the dysentery cultures themselves. This is the case; or it has fewer receptors that have to be satisfied before agglutination takes place. The same phenomenon is probably illustrated by our organism and typhoid bacilli in normal beef serum. There are agglutinins present in the serum active for both typhoid and "Y". Our organism, is however, agglutinated in much higher dilutions than the typhoid bacillus, showing that there is much more "Y" agglutinating substance present, or that "Y" is agglutinated with fewer receptors satisfied than is the typhoid bacillus.

The action of beef serum is important as it may be found to afford a practical means of differentiating true Shiga bacilli from organisms of the "Y" type. Shiga's bacillus as above noted does not agglutinate in beef serum, to an appreciable degree.

These facts brought out in regard to the serum reactions of "Y", dysentery, and typhoid bacilli have important practical bearings. Unless careful studies are made of all organisms resembling Shiga's bacillus, gross errors may occur in serum diagnoses based upon the use of such organisms in testing reactions; and errors may also occur in identifying such organisms themselves by simple tests against dysentery serum. This is illustrated by the fact that "Y" agglutinates better even than the true Shiga bacillus in dysentery serum, and unless true Shiga bacilli are tested against immune "Y" serum they may not be differentiated from each other. It is more than probable that organisms corresponding to "Y" have already been isolated and not recognized as distinct from Shiga's bacillus. This may then lead to the converse mistake of establishing the identity of a dysenteric or diarrhoeic attack with true dysentery by agglutinations obtained by the use of a bacillus differing from the supposed etiological organisms.

These remarks are not meant to convey the impression that "Y" itself is not or may not be found to be etiologically related to some form of dysenteric or diarrhoeic disease, but are intended to bring out the fallacy or relying solely upon serum reactions in identifying either disease or organism. It is fortunate, therefore, that the study of cultural characters has aided us in the recognition of differences in these organisms and may be of further service in the recognition and grouping of new organisms as they are discovered.

It seems to us in the face of our knowledge of the discrepancies in degree of agglutinability of such well-known organisms as typhoid bacilli, which not only show variations among the different cultures, but in the same species under practically non-determinable culture conditions, that we should hesitate before placing too much confidence in differences determined by serum reactions alone, but should endeavor in all cases by careful and extended study to establish their identity or dissimilarity by every cultural and biochemical test available.

Arguing from the analogy of our work on immune animal sera, an infection due to a bacillus of the "Y" species might, if tested against typhoid bacilli, give a reaction in a dilution considered diagnostic, and sera from both dysenteric and typhoid patients when tested against "Y", would certainly give reactions in high dilutions. Conversely, "Y" might be identified either with typhoid or Shiga bacilli if dependence were placed on serum reactions alone in its recognition.

Pathogenicity.—Our bacillus is pathogenic for both rabbits and guinea-pigs, but not markedly so. No characteristic lesions have so far been noted. Some hyperaemia of the small intestine is apparent. Rabbits may be readily accustomed to large doses of living cultures without showing a marked loss in weight.

As noted earlier in this paper, Lentz in a cultural study of a large number of true Shiga bacilli and other more or less closely allied organisms isolated from dysenteric patients, claims to have been able to separate by the use of a mannit litmus agar the cultures, which he designates as "Flexner I," "Flexner Manila" and "Strong," from the true bacillus of Shiga and Kruse. The results of his tests indicated that grown in this medium, Shiga's bacillus does not give rise to changes in the medium, with the exception of a decolorization of the medium in its lower layers, the medium remaining of the normal blue or deep purple in the upper section. In the media inoculated with the "Flexner" and "Strong" bacilli, the color changes to a distinct red due to acid production.

We have endeavored to repeat Lentz's experiments. The medium used by him in his earlier experiments was made according to the formula given by Drigalski for his typhoid isolation medium, with the substitution of mannit for the lactose. In Lentz's article on *Dysentery* in *Kolle* and *Wassermann's Handbuch der pathogenen Mikro-organismen* (p. 321), the method of preparation is somewhat simplified. This last method is the one followed by us.

At the present moment we are unable to say whether our culture "Flexner" is one of the organisms designated by Lentz as "Flexner I" or "Flexner Manila".

The tests of our culture "Flexner" on Lentz's medium do not agree with his published results.* Flexner's

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* Since writing the above, I have had the opportunity, through the kindness of Dr. Flexner, of examining the cultures "Flexner Manila (Harris)" and "Flexner Manila (Gray)" and Strong's Manila culture. These are the cultures examined by Martini and Lentz, and the culture "Flexner" examined by us, according to our tests, is not one of them. Both of Flexner's Manilla cultures, as well as that of Strong, differ from the true Shiga bacillus in fermenting mannit, as shown by acid production. Strong's bacillus seem to be identical with our organism "Y". Flexner's Manila culture, as well as one of his Baltimore cultures (sent to me by Dr. W. H. Park) is further differentiated from Shiga's bacillus and from our bacillus "Y" and Strong's culture by fermenting maltose. Saccharose is also fermented with acid production by Flexner's Manila cultures and also the culture "Baltimore." My tests also indicate that these bacilli will produce acid in the presence of dextrin. Their fermentation of saccharose and the absence of active motility separates them from B. typhosus. Their fermentation of maltose, saccharose and dextrin is slower than their action on dextrose and mannit, and may not be apparent for some days. Control saccharose tubes inoculated with B. typhosus show no change, so that this cannot be attributed to the presence of dextrose derived from the splitting of saccharose in the preparation of the medium. Control tubes of maltose and dextrose inoculated with Bacillus "Y" and Shiga's bacillus also remain blue and unchanged.

We have then, apparently, three groups of organisms. One represented by the true Shiga bacillus, fermenting dextrose and some other monosaccharids: one by our organism "Y", fermenting dextrose (monosaccharids) and the alcohol mannit: and finally a group represented by the more active fermenters, Flexner's Manila cultures and the culture "Baltimore," organisms which split dextrose, mannit, maltose, dextrin, and saccharose with the production of acid, as indicated by the reddening and coagulation of the serum-water sugar media.

This study shows plainly the inadvisability of relying upon superficial bacillus gives identically the same reaction in his litmus mannit agar as the results obtained when "Kruse" and "New Haven are tested. The culture medium of Lentz, which is used in tubes and inoculated by central puncture, in all three instances became slightly reddened below but remained blue at the surface. The medium in Lentz's experiments with Flexner's bacillus reddened.

Our bacillus "Y" and the organism "48" as well as true typhoid bacilli, when grown in the medium give rise to a reddening of the medium throughout its entire depth. These results were what we naturally expected from our knowledge of the metabolism of these organisms. "Kruse," "New Haven" and "Flexner" do not utilize mannit either in the presence or absence of oxygen or give rise to acid from it. Bacillus "Y" and "48" and typhoid bacilli ferment mannit with rapid production of acid, and hence redden the entire medium. This was to be expected from their fermentation tube reactions and the results of our experiments with serum-water plus mannit.

An explanation of these discrepant results may possibly, however, be found in the fact, which seems to have escaped the notice of both Drigalski and Lentz, that the medium to which they add sugars, such as mannit, lactose, etc., to be tested, is *not* glucose free. No mention is made of the removal of muscle sugar from the nutrient infusion used by them, nor is this recommended in the directions for preparing the medium. The presence of a fermentable substance, not mannit, in Lentz's medium, is clearly demonstrated by the reddening and possible subsequent clearing of the lower portion of the medium

characters or agglutination tests alone in the identification of an organism, or on the serum tests in the determination of the special character of a disease, and also lends support to our supposition that organisms differing from the true Shiga bacillus have been isolated and confounded with this organism.—*Hiss.*

when tested with our cultures "Kruse," "New Haven" and "Flexner" which do not ferment mannit. That the medium remains blue at the top may simply indicate that in the presence of oxygen the alkali production neutralized or exceeded the production of acid.

We have made up samples of the medium from sugar free meat infusion and find that in tests of cultures "Kruse," "New Haven" and "Flexner" no reddening of any portion of the medium occurs. Furthermore, when the medium is used soon after heating and oxygen driven off, the growth is confined to the surface, or upper parts of the inoculation line, since these organisms do not grow anaerobically in the presence of mannit in otherwise sugar free media. In tests of mannit fermenting organisms such as "Y," "48" and typhoid bacilli, the glucose free mannit medium is found reddened throughout, and growth has taken place along the entire length of the inoculation puncture.

None of the results of Lentz's sugar tests, although they may be roughly indicative, can be scientifically reliable so long as the medium used by him contains this original sugar, and the justice of our criticism of his method is evident in the discrepancies noted by Lentz* himself between the action of colon bacilli on media made by him and the results obtained by Drigalski with colon bacilli. Furthermore, slight differences in the initial reaction of the medium (alkali content) which are unavoidable with their method of neutralization and alkalinization, might also determine differences in their color reactions.

Resumé.

To review briefly: We have in this paper described an organism from a case of fatal diarrhœa. The organism agglutinates in high dilutions with the serum from dysentery patients and animals immunized with Shiga bacilli. Formerly this bacilli "Y" could not have been differentiated by valid culture tests from the bacillus of Shiga; and, the mannit test being unknown, might easily have been confounded with Shiga's organism unless its agglutinating reactions had been carefully studied in such a serum as that from typhoid immune animals, or from the normal beef, in neither of which the true Shiga bacillus agglutinates in appreciable dilutions.

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* See foot note by Lentz. *Zts. f. Hyg. 1902*, Bd. XLI, h. 3, pp. 560, 561.

The bacillus described by us is also closely related to B. typhosus, both in agglutinating reactions, and in the usually observed cultural characters, but can be separated from it by the absence of motility and by its reactions in the maltose and dextrin media employed by us.

This bacillus apparently differs from all hitherto described dysentery-like or "pseudodysentery" bacilli, in its agglutination in high dilutions of dysentery serum, an agglutination in some instances more marked than that shown by the true Shiga bacillus. A description of this organism—apart from its connection, which may or may not be etiological, with the case of diarrhoea—has seemed to us important, since tests of its ability to agglutinate—too often alone relied upon—might lead to its being confounded with Shiga's bacillus. A subsequent use of such an organism for serum diagnosis might thus give rise not only to confusion in determining the "specific" character of a disease, but to untoward results in the application of serum therapy.

Its etiological significance we have not been able to determine but its close physiological connection with the dysentery bacillus on one side, and the bacillus of typhoid fever on the other, make it not improbable that further research will show it to be associated etiologically with certain diarrhœic or dysenteric attacks.

Discussion.

Dr. David Bovaird gave details of the case from which the organism described by Dr. Hiss had been isolated. The patient was a child of about one year, who suffered from an attack of enterocolitis. The temperature was not high, never over one hundred. There was persistent diarrhoea, from four to six stools every day. For the most part they had been green and contained mucus. There had been no mention of any blood in the stools. The child lost strength progressively and died in two weeks. Dr. Bovaird considered that Dr. Hiss' results were of the utmost importance. He said that it was only a short time since the Society had listened to Dr. Flexner describe the finding of the bacillus of Shiga in approximately fifty cases of dysentery in children, and since that occasion there had been numerous reports of the finding of the bacillus in diarrhoeas of children in various parts of the country. Efforts had already been made to develop a serum which would be of use in the treatment of these cases. He had but recently read the report of the work of Gay, of the University of Pennsylvania, who thought he had been able to produce such a serum. Since, therefore, it was evident that we were approaching the treatment of some of these cases by sera, it became very important that the diagnosis in all cases should be very exact before such treatment was undertaken. Such observations as Dr. Hiss' were therefore of great value, in indicating a possible source of error. Further investigation would be required to de termine the full application of Dr. Hiss' observations. If the Shiga bacillus were found to be the specific cause of many of the diarrhoeas common in children, the association with the term dysentery would be a source of some difficulty and confusion. That term had not been seen in pediatric writings for some years, and there was no clear conception of the clinical picture which it should call up. Certainly there were marked differences betwen the diarrhoeas common in children during the summer and the condition in adults designated as dysentery. If it were consistent with the facts, it would be an advantage in discussion to employ the term colitis or enterocolitis, which would be much more definite and clear.

Dr. W. H. Park said that only the night before Dr. Smith had inoculated all these different bacilli in nutrient agar to which litmus and mannit had been added. There was no question that on this medium which had a trace of meat sugar, the Shiga bacillus and the Flexner New Haven culture stood out perfectly clearly from the rest in not having produced appreciable acid. Although the elimination of the meat sugar might be insisted on so as to judge what effect the bacilli had on mannit, yet the marked differences between these bacilli and all the others was just as important in showing differences between the bacilli as if the medium had contained only mannit. Dr. Park did not think it correct to speak of developing in this country a new serum for dysentery. Shiga had used the serum in a number of cases and attempts made here so far had been simply copies of what he had already done. Shiga himself had only employed the usual methods. He thought it was a mistake to go too fast in applying the results obtained by those working under Dr. Flexner at Baltimore, to ordinary summer diarrhoeas until it was proven whether all these bacilli were really essentially identical and also whether it might not be true, as seemed probable, that the conditions at the Wilson Sanatorium were unusual in the amount of infection which existed with dysentery-like bacilli.

Dr. Hiss said that he wished to say that the tubes of Lentz's medium shown contained media made according to Lentz's formula, and also mannit media made from sugar free infusion. If held against the light one could see that the sugar free tubes showed no growth except at the surface, and not along the line of inoculation.

Dr. E. Libman said that he thought there were several points in Dr. Hiss' paper deserving of corroboration. He had noticed as had Dr. Hiss that the medium described by Drigalski and Conradi was not made sugar free and he had therefore hesitated about using it. As regarded the value of agglutination reactions for the diagnosis of dysentery, he had examined a number of bloods from cases not having a history of dysentery to ascertain whether the reaction was specific; for he thought the reaction, if specific, could be used to establish the identity of certain conditions which appeared to be sequelae of dysentery (the patients at the time of observation not having evidences of dysentery). He had examined the blood from ten cases taken at random in the wards. The reaction was absent with the Flexner bacillus in all but two cases. One case of auto-intoxication gave a good reaction at 1–50; and a case of rheumatism gave a good reaction at 1–100 in twenty minutes. Possibly in higher dilutions the agglutination tests might have been specific. He was interested in Dr. Hiss' remarks about the occasional absence of clump reactions in low dilutions when present in high dilutions. He had. himself observed this with immune typhoid serum. This was an important point practically. He had examined the blood of two cases of typhoid fever which had given only a slight reaction at 1–20, but a complete reaction at 1–50 and 1–100. As only complete reactions could be considered in making the diagnosis of typhoid fever, he believed that when a blood does not react in low dilutions, higher dilutions should be tried. It seemed probable from the paper just read that just as in cases of paracolon infection the organisms showed variations, the same was true of dysentery, and in the same was the clinical picture of typhoid fever was due to a variety of organisms. Dr. Libman said he had recently seen a case of typhoid fever with perforation in which the Widal reaction was absent. Typhoid bacilli could not be found, but in the mesenteric lymphnodes, at the autopsy, the bacillus fecalis alkaligenes was found. . Serum reactions could not be tried. He did not wish to draw any conclusions from this finding, but believed it was of interest because this organism had been discovered by Petruschky alone or with the typhoid bacillus in cases having the clinical picture of typhoid fever.

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A METHOD OF SEPARATION OF COLONIES OF SHIGA'S BACILLUS FROM THE COLON BACILLUS.

E. K. DUNHAM, M.D.

Dr. Dunham gave an outline of studies of the influence of the physical properties of gelatin upon the appearance of colonies grown on plates. The physical characters chiefly noted were: the viscosity, the melting point, and the penetrability or spissitude. It seemed to him that a knowledge of the viscosity and the melting point was sufficient for a practical guide to the influence of the gelatin on colonies. To obtain a differentiation of colonies it was found desirable to grow them in a soft jelly, either by making a soft jelly to start with or by using a stiff jelly and incubating the plates at a high temperature. The size of the colonies was smaller if the plate was allowed to stand and harden at the room temperature before being put into the incubator, considerably larger if put at once into the incubator. In twenty-four hours the colonies prepared in the latter way were larger than colonies forty-eight hours old in a similar but softer jelly, grown at the same temperature, but chilled before incubation. In a soft jelly the typhoid bacillus formed threading colonies. The colon bacillus in a very soft jelly does not produce single colonies, but a collection of small colonies. The dysentery bacillus always produced a perfectly spherical colony except in jelly that was so soft as to be semi-fluid. For practical purposes the dysentery bacillus produced a perfectly spherical colony, easily distinguished from the colon and typhoid, more difficult to distinguish from the paratyphoid. It seemed therefore that in plating feces it would be very easy to ignore the colon bacillus and pay attention only to the spherical colonies. This would reduce the difficulty of finding the dysentery bacillus and could easily be done in twenty-four hours.

ON THE INTERPRETATIONS OF REACTIONS OF AGGLUTINATION AMONG THE BACILLI OF DYSENTERY.

WILLIAM H. PARK, M.D.

Dr. William H. Park gave the results of some experiments in agglutination reactions done by Dr. Collins and himself, in the course of which they had struck some things which he considered very remarkable. These were along the lines of Dr. Hiss' and Dr. Libman's remarks, except that they were perhaps more striking. He first spoke of normal goat serum and the necessity of knowing the serum agglutination results before the animal was inoculated. The serum from different goats varied widely. Experiments were made with the Shiga, Flexner Manila and New Haven bacilli, and with the bacillus isolated by himself and Dr. Dunham at Seal Harbor, Mt. Desert, and also with a bacillus furnished by Dr. Wollstein from one of a series of cases of dysentery occurring in the Foundling Asylum in New York City. In normal serum from goat (3) the Shiga, Flexner Manila and New Haven bacilli agglutinated perfectly up to 1–200 within from one to one and one-half hours, while the Seal Harbor bacillus refused absolutely to clump in any dilution above 1–10. After the goat had been inoculated with three injections of the Seal Harbor bacillus the tests showed that all the bacilli mentioned were clumped in dilutions somewhat above 1–200 except the Seal Harbor. This agglutinated in dilutions only up to 1–50. This at first seemed unexplainable until reference to the results of the normal serum tests already spoken of showed that the slight reaction of the Seal Harbor bacillus in the serum of goat (3), after moderate injections with it, was due to the fact that the goat originally had almost no agglutinating substance for this bacillus, while having much more for the others. Such experiences proved the necessity of knowing the properties of the animal's serum at the beginning, before injections of bacteria or blood were made. After five injections of Flexner's Baltimore cultures the horse serum clumped all the bacilli except the Shiga and Flexner New Haven cultures which did not clump at all in dilutions higher than 1–75. All the others clumped up to 1–1000. A bacillus obtained by Dr. Park from three persons suffering from chronic dysentery, which in sugar fermentation was closely allied to the colon bacillus, clumped in this Baltimore culture horse serum in dilutions up to 1–10,000.

Curiously enough this bacillus had clumped in every dysentery serum in which the Flexner cultures other than the New Haven were clumped. In two human typhoid immune sera the Shiga and New Haven cultures did not clump at all, while the New York, Manila and

Baltimore cultures clumped in 1–50 and pretty well in 1–100. In this serum the Seal Harbor and Tuckahoe bacilli fell in the Shiga group, as did the bacillus from the chronic dysentery case. Tests with serum from a patient with a staphylococcus abscess gave no reaction with the Shiga, New Haven or Seal Harbor cultures; but an absolute reaction in dilutions of 1–100 with the chronic dysentery, Baltimore, Wollstein, and colon bacilli. Throughout all the agglutination tests the Shiga and New Haven bacilli showed divergence from the others. They had not been agglutinated by the agglutinating substances produced by or acting upon the others. The results of the tests with the colon-like bacillus which agglutinated in dilutions of 1–10,000 in the serum of a horse immunized with Manilla and Baltimore dysentery bacilli seemed to show that simple agglutinations even in dilutions much higher than those effective upon the organism used to immunize the animals were not enough to prove relationship between bacteria. In alkaline peptone mannit litmus nutrient agar the New Haven, Tuckahoe and Shiga cultures did not change the blue color in twenty-four hours. In all the other cultures production of acid occurred. The Flexner Manila, Baltimore, Seal Harbor and New York cultures produced indol in twenty-four hours in peptone water, while the Shiga and New Haven cultures did not, even in fourteen day's growth. Both in indol and acid productions therefore, as in agglutination reactions, the Japan and New Haven cultures were separated from the Manila, Baltimore, New York and Seal Harbor cultures.

Discussion.

Dr. Charles Norris asked by what method Dr. Park had made these agglutination reactions and what limits he used in determining them. The results seemed to him very extraordinary. Had Dr. Park used the microscopic method? He had himself got hold of a highly immune serum but had never been able to obtain higher agglutination reactions than 1–100 or 1–150. By the microscopic method he had got reactions up to 1–300. He had been particularly surprised by Dr. Flexner's remarks that he had got agglutinations in dysentery cases up to 1–1,000. He had never been able to obtain any nearly so high. The thing might depend upon what one [illegible] agglutination reaction.

[illegible] said that with the goat serum the complete reactions were both in the test tube and hanging drop. The dilutions of the immunized horse serum were mostly tested by the hanging drop methods. Up to three or for hours the results obtained with the two methods were identical. For longer times the tube method gave the more accurate results. All the results were obtained within two or three hours, when the hanging drop was used, most of them within two hours. The complete precipitation of the bacilli in the tubes when agglutination took place was slow, requiring a number of hours. The cultures used were broth cultures, three to six hours old. Equal parts of the diluted serum and of the broth cultures were mixed together.

Dr. E. Libman asked whether Dr. Park had found any thread reactions. In his own experience, under certain conditions, the same organism after it had been grown for a length of time in various media would often change as regarded its reaction. He had observed a paracolon bacillus which at first gave only a thread reaction with the patient's blood and not with any other blood, but which after a time gave a clump reaction with almost any blood tried against it. He asked whether Dr. Park had tried the reactions against any large number of normal sera.

Dr. Park said that in testing blood sera from patients in dilutions of 1–10 to 1–50, he had found a great many thread reactions after twelve to eighteen hours. In high dilutions with the sera of immunized animals he had seldom found any.

Dr. P. H. Hiss said that in connection with Dr Park's remarks he was reminded of Shiga's latest article in which Shiga described the growth of his own bacilli in milk, by which means he got precisely the same reaction with the true Shiga bacillus as with the Flexner bacillus Dr. Hiss said that the results of his serum tests did not seem to show a correspondence between the Flexner bacillus which he had tested and the organisms "Y" which he had described. The "Y" had the power of agglutinating in very high dilutions, whereas the Flexner tested by him always agglutinated much less readily, in dysentery sera, and in other sera against which it was tested. He also said that the results of serum tests both in America and Europe indicated to him that one at least of Flexner's organisms did not react as did the Flexner organism tested by Dr. Park,—that usually it showed a markedly less agglutination than "Kruse," "Shiga" and "New Haven" in dysentery sera, from animals not immunized against itself.

Dr. Park said that he thought Dr. Hiss had misunderstood Shiga's article. He had had the same idea after first reading it, but after a careful re-reading, it became plain that Shiga said that the pro-agglutinoid zone was changed by the growth in milk, but not the agglutinating reactions. The Shiga bacillus still failed to remove the substances agglutinating the Flexner Manila culture and vice versa.

ON THE NATURE AND ORIGIN OF BLOOD PLATES.

L. B. GOLDHORN, M.D.

Dr. Goldhorn presented photographs and read a short paper on some observations which he had made on the formation of blood plates. After reviewing the literature, especially the work of Deetjen, he said that the reason that there were so many different opinions on the subject of blood plates was that in ordinary methods of heat fixation they were not well stained. Only in preparations in which very little heat was used or in which the fixation was chemical were the blood plates present in large numbers. They were more noticeable when staining dyes were used and were especially well demonstrated by the chromatin mixtures with eosin and polychrome methylene blue. One of the essentials was a thin smear. With the chromatin stain a central body could often be distinguished, of a bright red color sometimes compact, sometimes granular, surrounded by a central zone, always capable of being stained by basic dyes. He said there were several forms of blood plates, one devoid of chromatin granules; one with scattered granules; and one showing a compact mass of granules. In certain diseases abnormally large platelets were seen, especially in malaria. The platelets were regularly found in the blood in intimate relationship with the fibrin. Where there was no fibrin, there were no platelets. His conclusions were that the platelets were distinct and independent elements of the blood. They were not of a degenerative nature. There were several distinct types, all circular except for the fusiform variety. The size varied in health and disease. As to the origin of the plates the speaker said he had never had any evidence that they were derived from erythrocytes.

Discussion.

Dr. Ewing said that he had followed the discussion of the origin of blood plates for a number of years and had come to conclusions contrary in certain respects to those of Dr. Goldhorn. He had found that there was very convincing evidence to show that the blood plates originated from red blood cells and were sometimes stainable within them. He thought that there was abundant reason to believe that the platelets resulted from the extrusion of a nuclear substance from the red cells. By far the weight of evidence was in accord with this view. He thought that Dr. Goldhorn had brought out some very important facts. It seemed possible that there was more than one variety of blood plates in human blood, and Dr. Goldhorn's minute descriptions of their morphology were an important contribution favoring this view. He himself had been entirely unable to distinguish in human blood more than one variety.

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